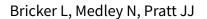


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Routine ultrasound in late pregnancy (after 24 weeks' gestation) (Review)



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[Intervention Review]

Routine ultrasound in late pregnancy (after 24 weeks' gestation)

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ABSTRACT

Background

Diagnostic ultrasound is used selectively in late pregnancy where there are specific clinical indications. However, the value of routine late pregnancy ultrasound screening in unselected populations is controversial. The rationale for such screening would be the detection of clinical conditions which place the fetus or mother at high risk, which would not necessarily have been detected by other means such as clinical examination, and for which subsequent management would improve perinatal outcome.

Objectives

To assess the effects on obstetric practice and pregnancy outcome of routine late pregnancy ultrasound, defined as greater than 24 weeks' gestation, in women with either unselected or low-risk pregnancies.

Search methods

We searched the Cochrane Pregnancy and Childbirth Group's Trials Register (31 May 2015) and reference lists of retrieved studies.

Selection criteria

All acceptably controlled trials of routine ultrasound in late pregnancy (defined as after 24 weeks).

Data collection and analysis

Three review authors independently assessed trials for inclusion and risk of bias, extracted data and checked them for accuracy.

Main results

Thirteen trials recruiting 34,980 women were included in the systematic review. Risk of bias was low for allocation concealment and selective reporting, unclear for random sequence generation and incomplete outcome data and high for blinding of both outcome assessment and participants and personnel. There was no difference in antenatal, obstetric and neonatal outcome or morbidity in screened versus control groups. Routine late pregnancy ultrasound was not associated with improvements in overall perinatal mortality. There is little information on long-term substantive outcomes such as neurodevelopment. There is a lack of data on maternal psychological effects.

Overall, the evidence for the primary outcomes of perinatal mortality, preterm birth less than 37 weeks, induction of labour and caesarean section were assessed to be of moderate or high quality with GRADE software. There was no association between ultrasound in late pregnancy and perinatal mortality (risk ratio (RR) 1.01, 95% confidence interval (CI) 0.67 to 1.54; participants = 30,675; studies = eight; $I^2 = 29\%$), preterm birth less than 37 weeks (RR 0.96, 95% CI 0.85 to 1.08; participants = 17,151; studies = two; $I^2 = 0\%$), induction of labour (RR 0.93, 95% CI 0.81 to 1.07; participants = 22,663; studies = six; $I^2 = 78\%$), or caesarean section (RR 1.03, 95% CI 0.92 to 1.15; participants = 27,461; studies = six; $I^2 = 54\%$). Three additional primary outcomes chosen for the 'Summary of findings' table were preterm birth less



than 34 weeks, maternal psychological effects and neurodevelopment at age two. Because none of the included studies reported these outcomes, they were not assessed for quality with GRADE software.

Authors' conclusions

Based on existing evidence, routine late pregnancy ultrasound in low-risk or unselected populations does not confer benefit on mother or baby. There was no difference in the primary outcomes of perinatal mortality, preterm birth less than 37 weeks, caesarean section rates, and induction of labour rates if ultrasound in late pregnancy was performed routinely versus not performed routinely. Meanwhile, data were lacking for the other primary outcomes: preterm birth less than 34 weeks, maternal psychological effects, and neurodevelopment at age two, reflecting a paucity of research covering these outcomes. These outcomes may warrant future research.

PLAIN LANGUAGE SUMMARY

Routine ultrasound in late pregnancy (after 24 weeks' gestation) to assess the effects on the infant and maternal outcomes

Ultrasound can be used as a clinical diagnostic tool in late pregnancy to assess the baby's condition when there are complications, or to detect problems which may not otherwise be apparent. If such problems are identified this may lead to changes in care and an improved outcome for babies. Carrying out scans on all women is however controversial. Screening all women may mean that the number of interventions is increased without benefit to mothers or babies. Although popular, women may not fully understand the purpose of their scan and may be either falsely reassured, or unprepared for adverse findings. Existing evidence shows that routine ultrasound, after 24 weeks' gestation, in low-risk or unselected women does not provide any benefit for the mother or her baby. Thirteen studies involving 34,980 women who were randomly selected to screening or a control group (no or selective ultrasound, or ultrasound with concealed results) contributed to the review. The quality of trials was satisfactory. There were no differences between groups in the rates of women having additional scans, antenatal admissions, preterm delivery less than 37 weeks, induction of labour, instrumental deliveries or caesarean section. Babies' birthweight, condition at birth, interventions such as resuscitation, and admission to special care were similar between groups. Infant survival, with or without congenital abnormalities, was no different with and without routine ultrasound screening in late pregnancy. None of the trials reported on the effect of routine ultrasound in late pregnancy on preterm birth less than 34 weeks, maternal psychology or mental development of babies when two years old.

The ultrasound scan protocols in each trial varied, as did the reasons for ultrasound scans after 24 weeks' gestation. The influence of first and second trimester ultrasounds is difficult to disentangle, and assessment of most measures at late pregnancy is based on gestational reference data, which rely on accurate gestational dating in early pregnancy. Trials were undertaken over a period of time covering early introduction into clinical practice to widespread use, during which time how to assess fetal size and well being ultrasonographically were still being debated. As ultrasound technology continues to advance and become more accessible, it is important to maintain a clear idea of its relevance. Ultrasound, being a clinical investigation, may be used to detect abnormality without the impact of such detection on clinical outcomes being full assessed. Exposure of the expectant mother to uncertainty and possible anxiety about the health of her baby has implications that may be far reaching. In addition, little is known about how the baby that was compromised in the uterus develops after birth and in the first years of life.



Summary of findings for the main comparison. Routine ultrasound > 24 weeks for pregnant women

Routine ultrasound > 24 weeks for pregnant women

Patient or population: women in late pregnancy (after 24 weeks' gestation) in both unselected populations and designated low-risk populations

Settings: Scandinavia, Northern Ireland, New Zealand, Australia and the United Kingdom **Intervention:** routine ultrasound > 24 weeks versus no/concealed/selective ultrasound

Outcomes	Illustrative comparative risks* (95% CI)		Relative effect (95% CI)	No of partici- pants	Quality of the evidence	Comments
	Assumed risk	Corresponding risk	(33 /0 Ci)	(studies)	(GRADE)	
	Control	Routine ultrasound > 24 weeks				
Perinatal mortality	Study population		RR 1.01 - (0.67 to 1.54)	30675 (8 studies)	⊕⊕⊕⊝ moderate ¹	
	6 per 1000	6 per 1000 (4 to 9)	(6.6. to 2.6.)	(0 000 00)	moderate	
	Moderate					
	5 per 1000	5 per 1000 (3 to 8)				
Preterm delivery < 37 weeks' gestation	Study population		RR 0.96 - (0.85 to 1.08)	17151 (2 studies)	⊕⊕⊕⊕ high	
37 weeks gestation	59 per 1000	57 per 1000 (50 to 64)	(0.03 to 1.00)	(2 studies)	5	
	Moderate					
	60 per 1000	58 per 1000 (51 to 65)				
Induction of labour	Study population		RR 0.93 - (0.81 to 1.07)	22663 (6 studies)	⊕⊕⊕⊝ moderate ²	
	238 per 1000	222 per 1000 (193 to 255)	(0.61 to 1.07)	(o studies)	moderate 2	
	Moderate					
	242 per 1000	225 per 1000				

		(196 to 259)				
Caesarean section Study population			RR 1.02 (0.97 to 1.09)	27461 (6 studies)	⊕⊕⊕⊕ high	
	139 per 1000	142 per 1000 (135 to 152)	(0.97 to 1.09) (6 studies) high			
	Moderate					
	133 per 1000	136 per 1000 (129 to 145)				
Preterm delivery less than 34 weeks	Study population		Not estimable	0 (0)	Not estimable	None of the included tri- als in this review collected
- Weeks	See comment (0)			data for this outcome.		
Maternal psycho- logical effects	Study population		Not estimable	0 (0)	Not estimable	None of the included tri- als in this review collected
	See comment		(0)			data for this outcome.
Neurodevelopment at age 2	Study population		Not estimable	0 (0)	Not estimable	None of the included tri- als in this review collected
	See comment		(4)			data for this outcome.

^{*}The basis for the **assumed risk** (e.g. the median control group risk across studies) is provided in footnotes. The **corresponding risk** (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI). **CI:** Confidence interval; **RR:** Risk ratio

GRADE Working Group grades of evidence

High quality: Further research is very unlikely to change our confidence in the estimate of effect.

Moderate quality: Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate.

Low quality: Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate.

Very low quality: We are very uncertain about the estimate.

 $^{^{1}\,\}mbox{Wide}$ confidence interval crossing the line of no effect. RR 1.01 (0.67 to 1.54)

² Statistical heterogeneity I² = 78%



BACKGROUND

Description of the condition

Fetal growth/size

Small-for-gestational age (SGA) fetuses are at greater risk of stillbirth, birth hypoxia, neonatal complications in the perinatal period, impaired neurodevelopment and cerebral palsy in childhood, and non-insulin dependent diabetes and hypertension in adult life (Barker 1993). The majority of these small infants are not diagnosed until delivery (Leeson 1997), and detecting these fetuses prenatally remains a priority of antenatal care (Lindqvist 2005). Methods of detecting SGA fetuses include antenatal clinical examination, measurement of symphysisfundal height, fetal anthropometry and ultrasound estimated fetal weight. Harding 1995 demonstrated that symphysisfundal height measurements perform relatively poorly compared with ultrasound abdominal circumference measurements, while Hendrix 2000 suggested that, for term pregnancies, clinical examinations provide more accurate estimates of birthweight than ultrasound. A combined approach of screening with symphysisfundal height measurement, complemented with ultrasoundderived fetal abdominal circumference if failing growth is suspected, has been advocated. Holmes 1996 cautions that small size should be viewed as a clinical sign, and not a diagnosis, as a number of small fetuses are not at risk of an adverse outcome. Furthermore, the use of ultrasound to detect the SGA fetus is dogged by a number of complicating factors, including the lack of defined thresholds for normality versus abnormality, its dependence on accurate gestational dating, the fact that the assessment of growth velocity (serial measurements) may be more valuable clinically than a single estimate of size, and differences due to other factors, namely, maternal ethnicity and parity, fetal gender and environmental factors (Altman 1989). A more recent study has found that maternal ethnicity may not be as important as previously thought as fetal growth and newborn length are similar across diverse geographical settings when mothers' nutritional and health needs are met, and environmental constraints on growth are low (Villar 2014). A previous systematic review of routine late pregnancy anthropometry concluded that despite increased intervention (admission to hospital and induction of labour), there was no identifiable benefit in fetal outcome (Neilson 1995).

Another clinical concern is with the large-for-gestational-age (LGA) fetus. These babies are at increased risk of perinatal morbidity and mortality, which arises mainly from birth injury and asphyxia; their mothers are at increased risk of cephalo-pelvic disproportion and its sequelae, and operative delivery and the associated morbidity. Our ability to detect fetal macrosomia (large baby) antenatally by clinical examination remains limited (Lurie 1995), and the antenatal prediction of fetal macrosomia is associated with a marked increase in caesarean births, without a significant reduction in the incidence of shoulder dystocia or fetal injury (Weeks 1995). This is because most cases of shoulder dystocia and birth trauma occur in non-macrosomic infants (Gonen 1996). Hence, the value of detecting LGA fetuses by routine ultrasound in late pregnancy is questionable.

Amniotic fluid

Fetal urine is the major source of amniotic fluid in the latter half of pregnancy (Brace 1989). Decreased amniotic fluid volume (oligohydramnios) in the absence of ruptured membranes or fetal anomalies is thought to be associated with chronic fetal compromise and redistribution of regional blood flow leading to a reduction in fetal renal blood flow, fetal oliguria (low output of urine) and thus less amniotic fluid. Increased amniotic fluid volume (polyhydramnios) occurs as a result of overproduction (polyuria in fetuses of diabetic mothers, rare placental tumours), decreased turnover (congenital anomalies affecting fetal swallowing), or unknown aetiology. Both oligohydramnios and polyhydramnios can be diagnosed by ultrasound measurement of maximum pool depth, two-diameter amniotic fluid pocket or amniotic fluid index (the sum of the vertical maximum pool depths in four quadrants), and applying the result to normal reference ranges. While in highrisk pregnancies, such as postdate pregnancy, the measurement of amniotic fluid volume may have bearing on management decisions, there is some debate about the best measurement method, and the clinical significance of the available reference ranges, which compounds the uncertainty about the effect on perinatal outcome of detecting amniotic fluid abnormalities.

The placenta

Placenta praevia occurs in 0.5% of pregnancies and is associated with considerable risk to both mother and fetus. Ultrasound is the best available method for locating the placental position (Neilson 1989). Only 10% of low placentas at second trimester scan remain low at term (Rizos 1979). However, in most pregnancies with placenta praevia, a clinical indication for diagnostic ultrasound will arise such as antepartum haemorrhage and fetal malpresentation, and therefore the role of screening for placenta praevia is debatable.

Grannum 1979 described a classification system to grade the placental texture appearances on ultrasound imaging, and suggested a correlation between maturational changes of the placenta as seen on ultrasound and fetal pulmonic maturity. This was not confirmed in further study, but an association between 'mature' appearances at earlier gestations with maternal smoking and placental dysfunction was postulated. Therefore, the knowledge of placental appearances in late pregnancy could, in theory, result in care leading to improved perinatal outcome (Abramowicz 2007).

Structural fetal abnormalities

A number of structural fetal abnormalities may manifest later in pregnancy. These include craniospinal abnormalities (microcephaly and hydrocephaly), gastrointestinal abnormalities (intestinal obstruction and atresia), urinary tract abnormalities, and some skeletal abnormalities (Chitty 1995). It has been suggested that the value of detecting fetal structural abnormalities before birth allows for the optimal timing and mode of delivery leading to improved management and outcome. However, a report of a Working Party of the Royal College of Obstetricians and Gynaecologists on Ultrasound Screening for Fetal Abnormalities (RCOG 1997), stated that further research is required to evaluate whether prior identification of an abnormality before birth, particularly those amenable to intrauterine procedures and neonatal surgery, is advantageous in both the short and long term.

Fetal presentation

Some fetal malpresentations (e.g. breech) go undetected during routine antenatal care but would be identified by routine ultrasound in late pregnancy. In a retrospective case review, Nwosu



1993 showed that babies undiagnosed as a breech were not subject to increased morbidity and mortality compared with a breech diagnosed prior to labour. This highlights the uncertainty about the clinical value of routine ultrasound screening for fetal malpresentation.

Description of the intervention

Diagnostic ultrasound is a sophisticated electronic technology, which utilises pulses of high frequency sound. The transducer, which is moved across the area to be examined, emits the pulses of ultrasound which propagate through the tissues, and some are reflected back to the transducer which converts these returning echoes into electronic signals. Tissue interface characteristics determine the strength of the returning echo. Signals are processed by a computer which displays each echo in both strength and position as an image on a screen.

Safety

The use of routine pregnancy ultrasound needs to be considered in the context of potential hazards. Theoretically, some ultrasonic energy propagated through tissue is converted to heat, and biological effects of ultrasound have been observed in laboratory experiments. However, these effects have been produced using continuous wave ultrasound with long 'dwell' time (time insonating one area) and high power output. Diagnostic ultrasound is pulsed wave (short pulses of sound propagation), and most modern machines have inbuilt safety features, so that safe power output limits cannot be exceeded. Operators are advised to apply the ALARA principle (as low as reasonably attainable) to the ultrasound power output used (EFSUMB 1995), and to ensure time taken for an examination, including the 'dwell' time over a specific target, is kept to a minimum. However, there is some evidence that operators' knowledge about safety may not be accurate (Sheiner 2007). At present, there is no clear epidemiological evidence that ultrasound examination during pregnancy is harmful, but no firm conclusion has been reached from available data (see Cochrane review: Ultrasound for fetal assessment in early pregnancy (Whitworth 2010)), and therefore, continual vigilance is necessary. This is particularly important in a context where scans are increasingly being carried out for non-medical reasons, and where there is a paucity of information on the number of scans women actually receive as a part of their antenatal care (ACOG 2004). Apart from the physics of ultrasound, the potential harm of misdiagnosis and unnecessary intervention, such as unnecessary late preterm birth should also be considered.

Cost and maternal psychological effects

There have been few studies evaluating the cost effectiveness of ultrasound scans (Henderson 2002). While there is some information on the direct costs of ultrasound examinations, there is much less on indirect cost (e.g. the costs of associated counselling, follow-up tests and related interventions, and indirect costs to women). Further, there is relatively little information on the psychological impact of ultrasound on women and their families (partners are frequently present for scans). Scans are popular with women, but women may not fully understand the purpose of their scan, and may be either falsely reassured or unprepared for adverse findings (Garcia 2002).

How the intervention might work

Diagnostic ultrasound is used selectively in late pregnancy where there are specific clinical indications, such as antepartum haemorrhage or clinical concern that the fetus may be poorly grown. However, the value of routine late pregnancy ultrasound screening in unselected populations is controversial. The rationale for such screening would be the detection of clinical conditions which place the fetus or mother at high risk, which would not necessarily have been detected by other means such as clinical examination, and for which subsequent management would improve perinatal outcome.

Why it is important to do this review

This is an ongoing issue that must be addressed. Furthermore, as ultrasound technology continues to advance and become more accessible it is important to maintain a clear idea of its relevance. In particular, classically fetal size or amniotic fluid volume are known to be clinical signs which can be readily detected by ultrasound, however, how much this information improves outcomes is not well established. By contrast, placental location is known to pose considerable risk to both mother and fetus and ultrasound remains the best available method of early determination of placental location (Neilson 1989). There remain inconsistencies in the available evidence regarding ultrasound in late pregnancy. Ultrasound, being a clinical investigation, may be used to detect abnormality without the impact of such detection on clinical outcomes being fully assessed. Furthermore, there are issues with the use of ultrasound including cost, access, maternal psychological effects and the need for continuous reassessment of its safety. Hence, it is important that this review evaluates the impact the use of ultrasound in late pregnancy on clinical outcomes.

OBJECTIVES

To assess the effects on obstetric practice and pregnancy outcome of routine late pregnancy ultrasound, defined as greater than 24 weeks' gestation, in women with either unselected or low-risk pregnancies.

METHODS

Criteria for considering studies for this review

Types of studies

All acceptably controlled trials of routine ultrasound in late pregnancy (after 24 weeks). Due to an anticipated paucity of randomised controlled trials, we considered quasi-randomised trials for inclusion. Routine ultrasound in early pregnancy (Whitworth 2010) has been considered in a previous Cochrane review. Routine doppler ultrasound in normal pregnancy has also been considered in a separate review (Alfirevic 2015).

Types of participants

Women in late pregnancy (after 24 weeks' gestation) in both unselected populations and designated low-risk populations.

Types of interventions

Routine ultrasound examination in late pregnancy (after 24 weeks' gestation) to assess one, some, or all of the following: fetal



size; amniotic fluid volume; placental site; placental grading; fetal structural anatomy; fetal presentation.

Types of outcome measures

Primary outcomes

- 1. Induction of labour.
- 2. Caesarean section.
- 3. Perinatal mortality.
- 4. Preterm delivery less than 34 weeks.
- 5. Preterm delivery less than 37 weeks (non-prespecified).
- 6. Neurodevelopment at age two.
- 7. Maternal psychological effects.

Secondary outcomes

Interventions

- 1. Antenatal admission to hospital.
- 2. Antenatal fetal monitoring (kick count chart; cardiotocography; biophysical profile; Doppler ultrasound; further ultrasound).

Intention to deliver

 Operative delivery (elective caesarean section (CS); emergency CS; instrumental vaginal delivery; CS for distress; CS for distress antepartum; CS for distress intrapartum).

Perinatal outcomes

- 1. Gestational age at birth.
- 2. Birthweight (mean and standard deviation).
- 3. Birthweight less than 10th percentile.
- 4. Birthweight less than third percentile.
- 5. Low birthweight (less than 2.5 kg).
- 6. Very low birthweight (less than 1.5 kg).
- 7. Need for resuscitation.
- 8. Need for ventilation.
- 9. Admission to special care baby unit and average stay.
- 10.Low Apgar score (less than seven at five minutes).

Neonatal outcomes

- Acute neonatal problems (hypoxic ischaemic encephalopathy; necrotising enterocolitis; intraventricular haemorrhage (IVH); IVH with cystic periventricular leukomalacia; pulmonary haemorrhage).
- 2. Early neonatal death (in first week of life).
- 3. Late neonatal death (from one to four weeks).
- 4. Infant death (one month to one year).

Maternal outcomes

- 1. Psychological effects (including stress, anxiety, depression, quality of life, satisfaction).
- 2. Detection of: (major anomaly before birth; malpresentation before labour).

Furthermore, the following non-prespecified outcome measures were used.

- 1. Post-term delivery greater than 42 weeks.
- 2. Birthweight less than 5th percentile.

- 3. Moderate neonatal morbidity (includes any of the following: presumed neonatal sepsis, oxygen required greater than 48 hours, necrotising enterocolitis without perforation, grade I or II IVH, fracture of clavicle or other bones, facial nerve injury, brachial plexus injury, stay greater than five days in the special care nursery).
- 4. Severe neonatal morbidity (includes any of the following: grade IV retinopathy of prematurity, bronchopulmonary dysplasia, mechanical ventilation greater than 48 hours, intestinal perforation due to necrotising enterocolitis, grade III or IV IVH, subdural or cerebral haemorrhage, spinal cord injury, neonatal seizures, placement of chest tube, documented neonatal sepsis, stay more than 30 days in the special care nursery).
- 5. Neonatal deaths.
- 6. Stillbirths.
- 7. Perinatal mortality of twins.
- 8. Perinatal mortality (excluding congenital abnormalities).
- 9. Stillbirths (excluding congenital abnormalities).
- ${\bf 10. Neon at al\ deaths\ (excluding\ congenital\ abnormalities)}.$
- 11. Number of days in hospital.

Search methods for identification of studies

The following methods section of this review is based on a standard template used by the Cochrane Pregnancy and Childbirth Group.

Electronic searches

We searched the Cochrane Pregnancy and Childbirth Group's Trials Register by contacting the Trials Search Co-ordinator (31 May 2015).

The Cochrane Pregnancy and Childbirth Group's Trials Register is maintained by the Trials Search Co-ordinator and contains trials identified from:

- monthly searches of the Cochrane Central Register of Controlled Trials (CENTRAL);
- 2. weekly searches of MEDLINE (Ovid);
- 3. weekly searches of Embase (Ovid);
- 4. monthly searches of CINAHL (EBSCO);
- handsearches of 30 journals and the proceedings of major conferences:
- 6. weekly current awareness alerts for a further 44 journals plus monthly BioMed Central email alerts.

Details of the search strategies for CENTRAL, MEDLINE, Embase and CINAHL, the list of handsearched journals and conference proceedings, and the list of journals reviewed via the current awareness service can be found in the 'Specialized Register' section within the editorial information about the Cochrane Pregnancy and Childbirth Group.

Trials identified through the searching activities described above are each assigned to a review topic (or topics). The Trials Search Coordinator searches the register for each review using the topic list rather than keywords.

Searching other resources

We searched the reference lists of retrieved studies.

We did not apply any language or date restrictions.



Data collection and analysis

For methods used in the previous version of this review, see Bricker 2008

For this update, the following methods were used for assessing the seven reports that were identified as a result of the updated search.

The following methods section of this review is based on a standard template used by the Cochrane Pregnancy and Childbirth Group.

Selection of studies

Two review authors independently assessed for inclusion all the potential studies identified as a result of the search strategy. We resolved any disagreement through discussion or, if required, we consulted the third review author.

Data extraction and management

We designed a form to extract data. For eligible studies, two review authors extracted the data using the agreed form. We resolved discrepancies through discussion or, if required, we consulted the third review author. Data were entered into Review Manager software (RevMan 2014) and checked for accuracy.

When information regarding any of the above was unclear, we planned to contact authors of the original reports to provide further details.

Assessment of risk of bias in included studies

Two review authors independently assessed risk of bias for each study using the criteria outlined in the *Cochrane Handbook* for *Systematic Reviews of Interventions* (Higgins 2011). Any disagreement was resolved by discussion or by involving a third assessor.

(1) Random sequence generation (checking for possible selection bias)

We described for each included study the method used to generate the allocation sequence in sufficient detail to allow an assessment of whether it should produce comparable groups.

We assessed the method as:

- low risk of bias (any truly random process, e.g. random number table; computer random number generator);
- high risk of bias (any non-random process, e.g. odd or even date of birth; hospital or clinic record number);
- unclear risk of bias.

(2) Allocation concealment (checking for possible selection bias)

We described for each included study the method used to conceal allocation to interventions prior to assignment and assessed whether intervention allocation could have been foreseen in advance of, or during recruitment, or changed after assignment.

We assessed the methods as:

- low risk of bias (e.g. telephone or central randomisation; consecutively numbered sealed opaque envelopes);
- high risk of bias (open random allocation; unsealed or nonopaque envelopes, alternation; date of birth);

· unclear risk of bias.

(3.1) Blinding of participants and personnel (checking for possible performance bias)

We described for each included study the methods used, if any, to blind study participants and personnel from knowledge of which intervention a participant received. We considered that studies were at low risk of bias if they were blinded, or if we judged that the lack of blinding unlikely to affect results. We assessed blinding separately for different outcomes or classes of outcomes.

We assessed the methods as:

- low, high or unclear risk of bias for participants;
- low, high or unclear risk of bias for personnel.

(3.2) Blinding of outcome assessment (checking for possible detection bias)

We described for each included study the methods used, if any, to blind outcome assessors from knowledge of which intervention a participant received. We assessed blinding separately for different outcomes or classes of outcomes.

We assessed methods used to blind outcome assessment as:

· low, high or unclear risk of bias.

(4) Incomplete outcome data (checking for possible attrition bias due to the amount, nature and handling of incomplete outcome data)

We described for each included study, and for each outcome or class of outcomes, the completeness of data including attrition and exclusions from the analysis. We stated whether attrition and exclusions were reported and the numbers included in the analysis at each stage (compared with the total randomised participants), reasons for attrition or exclusion where reported, and whether missing data were balanced across groups or were related to outcomes. Where sufficient information was reported, or could be supplied by the trial authors, we planned to re-include missing data in the analyses which we undertook.

We assessed methods as:

- low risk of bias (e.g. no missing outcome data; missing outcome data balanced across groups);
- high risk of bias (e.g. numbers or reasons for missing data imbalanced across groups; 'as treated' analysis done with substantial departure of intervention received from that assigned at randomisation);
- · unclear risk of bias.

(5) Selective reporting (checking for reporting bias)

We described for each included study how we investigated the possibility of selective outcome reporting bias and what we found.

We assessed the methods as:

 low risk of bias (where it is clear that all of the study's prespecified outcomes and all expected outcomes of interest to the review have been reported);



- high risk of bias (where not all the study's pre-specified outcomes have been reported; one or more reported primary outcomes were not pre-specified; outcomes of interest are reported incompletely and so cannot be used; study fails to include results of a key outcome that would have been expected to have been reported);
- · unclear risk of bias.

(6) Other bias (checking for bias due to problems not covered by (1) to (5) above)

We described for each included study any important concerns we had about other possible sources of bias.

(7) Overall risk of bias

We made explicit judgements about whether studies were at high risk of bias, according to the criteria given in the *Handbook* (Higgins 2011). With reference to (1) to (6) above, we planned to assess the likely magnitude and direction of the bias and whether we considered it is likely to impact on the findings. We explored the impact of the level of bias through undertaking sensitivity analyses - see Sensitivity analysis.

Assessment of the quality of the evidence

For this update the quality of the evidence was assessed using the GRADE approach (Schunemann 2009). We assessed the quality of the body of evidence relating to the following outcomes for the main comparison, routine ultrasound > 24 weeks versus no/concealed/selected ultrasound > 24 weeks.

- 1. Induction of labour.
- 2. CS.
- 3. Perinatal mortality.
- 4. Preterm delivery less than 34 weeks.
- 5. Preterm delivery less than 37 weeks.
- 6. Neurodevelopment at age two.
- 7. Maternal psychological effects.

GRADE profiler (GRADE 2014) was used to import data from Review Manager 5.3 (RevMan 2014) in order to create a 'Summary of findings' table. A summary of the intervention effect and a measure of quality for each of the above outcomes was produced using the GRADE approach. The GRADE approach uses five considerations (study limitations, consistency of effect, imprecision, indirectness and publication bias) to assess the quality of the body of evidence for each outcome. The evidence can be downgraded from 'high quality' by one level for serious (or by two levels for very serious) limitations, depending on assessments for risk of bias, indirectness of evidence, serious inconsistency, imprecision of effect estimates or potential publication bias.

Measures of treatment effect

Dichotomous data

For dichotomous data, we presented results as summary risk ratio with 95% confidence intervals.

Continuous data

We used the mean difference if outcomes were measured in the same way between trials. We planned to use the standardised mean

difference to combine trials that measured the same outcome, but used different methods.

Unit of analysis issues

Cluster-randomised trials

For this update there were no cluster-randomised trials of relevance found. If in future updates we find relevant cluster-randomised trials, we will include these in the analyses along with individuallyrandomised trials. We will adjust their sample sizes or standard errors using the methods described in the Handbook [Section 16.3.4 or 16.3.6] using an estimate of the intracluster correlation coefficient (ICC) derived from the trial (if possible), from a similar trial or from a study of a similar population. If we use ICCs from other sources, we will report this and conduct sensitivity analyses to investigate the effect of variation in the ICC. If we identify both cluster-randomised trials and individually-randomised trials, we plan to synthesise the relevant information. We will consider it reasonable to combine the results from both if there is little heterogeneity between the study designs and the interaction between the effect of intervention and the choice of randomisation unit is considered to be unlikely.

We will also acknowledge heterogeneity in the randomisation unit and perform a sensitivity analysis to investigate the effects of the randomisation unit.

Cross-over trials

We have not included cross-over trials in this review because we do not consider this trial design appropriate to answer the review question.

Other unit of analysis issues

We have included three trials with multiple pregnancies in the cohort in this review. One outcome in the first comparison, routine ultrasound > 24 weeks versus no/concealed/selective ultrasound included the outcome of perinatal mortality (twins). Ideally when including multiple pregnancies analyses should be adjusted for clustering to take into account the non-independence of babies from the same pregnancy (Gates 2004), as when considering babies from a multiple pregnancy it is important to note they are more likely to have similar outcomes than babies from different pregnancies. If this adjustment is made confidence intervals are likely to be wider. We did not adjust for clustering in this review because the number of multiple pregnancies included is small and adjusting would make little difference to the findings and conclusion.

Dealing with missing data

For included studies, we noted levels of attrition. In future updates, if more eligible studies are included, the impact of including studies with high levels of missing data in the overall assessment of treatment effect will be explored by using sensitivity analysis.

For all outcomes, analyses were carried out, as far as possible, on an intention-to-treat basis, i.e. we attempted to include all participants randomised to each group in the analyses. The denominator for each outcome in each trial was the number randomised minus any participants whose outcomes were known to be missing.



Assessment of heterogeneity

We assessed statistical heterogeneity in each meta-analysis using the Tau², I² and Chi² statistics. We regarded heterogeneity as substantial if an I² was greater than 30% and either the Tau² was greater than zero, or there was a low P value (less than 0.10) in the Chi² test for heterogeneity. Had we identified substantial heterogeneity (above 30%), we planned to explore it by pre-specified subgroup analysis (see Subgroup analysis and investigation of heterogeneity).

Assessment of reporting biases

In future updates, if there are 10 or more studies in the metaanalysis, we will investigate reporting biases (such as publication bias) using funnel plots. We will assess funnel plot asymmetry visually. If asymmetry is suggested by a visual assessment, we will perform exploratory analyses to investigate it.

Data synthesis

We carried out statistical analysis using the Review Manager software (RevMan 2014). We used fixed-effect meta-analysis for combining data where it was reasonable to assume that studies were estimating the same underlying treatment effect: i.e. where trials were examining the same intervention, and the trials' populations and methods were judged sufficiently similar.

If there was clinical heterogeneity sufficient to expect that the underlying treatment effects differed between trials, or if substantial statistical heterogeneity was detected, we used random-effects meta-analysis to produce an overall summary, if an average treatment effect across trials was considered clinically meaningful. The random-effects summary was treated as the average range of possible treatment effects and we discussed the clinical implications of treatment effects differing between trials. If the average treatment effect was not considered clinically meaningful, we did not combine trials. Where we used random-effects analyses, the results were presented as the average treatment effect with 95% confidence intervals, and the estimates of Tau² and I².

Subgroup analysis and investigation of heterogeneity

We did not conduct subgroup analysis for this update of the review. If in future updates we identify substantial heterogeneity, we will investigate it using subgroup analyses or sensitivity analyses. Possible subgroups include those with comparable first and/or second trimester ultrasonography, or studies conducted within a certain timeframe to account for changes in technology, or studies which include a management algorithm based on ultrasound findings. We will consider whether an overall summary is meaningful, and if it is, we will use random-effects analysis to produce it.

Only the seven primary outcome measures will be used for subgroup analysis. We will assess subgroup differences by interaction tests available within RevMan (RevMan 2014). We will report the results of subgroup analyses quoting the Chi² statistic and P value, and the interaction test I² value.

Sensitivity analysis

We carried out sensitivity analyses to explore the effect of trial quality assessed by concealment of allocation, high attrition rates, or both, with poor quality studies being excluded from the analyses in order to assess whether this made any difference to the overall result.

RESULTS

Description of studies

Ultrasound examination options differed between trials, with some offering no routine scans at any time in pregnancy to the control group, some offering routine scans to all participants earlier in pregnancy (before 24 weeks' gestation), and some offering routine scan at all stages of the trial, but only revealing results of late pregnancy ultrasound (after 24 weeks' gestation) for the study groups.

Four trials (Alesund 1999 (Norway); Belanger 1996 (USA); RADIUS 1993 (USA); Trondheim 1984 (Norway)), offered routine ultrasound in the second and third trimesters versus selective ultrasound. In two trials (New Zealand 1993; Skrastad 2013 (Norway)), all women had second trimester ultrasound scans, and only the study group underwent a further third trimester ultrasound. In the Belfast 2003 (UK) trial, all women had a first trimester scan while the study group had additional scans at 30 to 32 weeks and 36 to 37 weeks. In the Glasgow 1984 (UK) trial, all women were offered second and third trimester ultrasound scans, but the results of the third trimester ultrasound were revealed only for the study group. In the Peterborough 1987 (UK) trial, all women had routine second and third trimester ultrasound scans, but placental grading at the third trimester ultrasound was revealed only for the study group. In two trials (Ellwood 1997 (Australia); Perth 1993 (Australia)), all women had routine second trimester ultrasound scans, and only the study group was offered serial ultrasound screening thereafter. In the Wladimiroff 1980 trial, all women underwent routine antenatal care, then only the study group was offered a single ultrasound to assess fetal chest area at 32 to 36 weeks.

The trials evaluated different aspects of third trimester ultrasound. Three trials (Glasgow 1984 (UK); New Zealand 1993; Wladimiroff 1980), addressed ultrasound screening for 'small for dates'. The Peterborough 1987 (UK) trial addressed the value of placental grading as an adjunct to routine third trimester ultrasound scan. The Belfast 2003 trial examined the impact of two third trimester scans which assessed liquor volume, fetal weight and placental maturity. The Skrastad 2013 trial assessed the impact of one third trimester scan which assessed fetal anatomy. The RADIUS 1993 (USA) trial was the only study that reported in detail, detection of fetal abnormalities at routine third trimester ultrasound scan. The Perth 1993 (Australia) trial combined repeated ultrasound scan for fetal biometry and amniotic fluid assessment with Doppler ultrasound, and the data were therefore analysed in a separate comparison (serial ultrasound and Doppler ultrasound versus selective ultrasound), and were also included in another Cochrane review entitled 'Fetal and umbilical Doppler ultrasound in normal pregnancy' (Alfirevic 2010). The Ellwood 1997 trial also compared repeated ultrasound scans with routine second trimester ultrasound only.

The results of the review should be considered in the light of these different factors, as the specific nature of the ultrasound regimens may have had some effect on the outcome measures.



Childhood developmental outcomes were measured in the Belanger 1996 and Perth 1993 studies as well as in the Alesund and Trondheim trials (the longer-term outcomes from the latter two trials have been combined (Norway 1992)).

Results of the search

The search was updated in August 2014 and seven new reports were identified. Two new trials were included. Two reports were additional publications for a previously included trial, one report was excluded, and two reports on currently active trials have been placed in ongoing studies. Finally, two studies previously excluded for no data have been moved to included studies because it is no longer the practice to exclude otherwise eligible trials based on a lack of outcome data alone (Belanger 1996; Wladimiroff 1980).

Included studies

See Characteristics of included studies tables below.

Thirteen trials comprising 34,980 women were included in the review (Alesund 1999; Belanger 1996; Belfast 2003; Ellwood 1997; Glasgow 1984; New Zealand 1993; Perth 1993; Norway 1992; Peterborough 1987; Skrastad 2013; RADIUS 1993; Trondheim 1984;

Wladimiroff 1980). Longer-term outcomes from the Alesund 1999 and Trondheim 1984 trials have been combined and described in a series of papers by Salvesen and colleagues (Norway 1992); this trial does not contribute to the total number of women above because long-term outcomes were measured in the children of women recruited to the original trials. Three trials meeting the inclusion criteria (Belanger 1996; Norway 1992; Wladimiroff 1980) contribute no data to the review outcomes.

Excluded studies

Seven trials were excluded after full-text review. Two assessed the accuracy of ultrasound in predicting outcomes in a non-clinical context (Arzola 2013; Hendrix 2000), two were not undertaken (Morrison 1992; Ong 2001), and three included populations which were not low risk (Owen 1994; Secher 1986; Secher 1987). See table of Characteristics of excluded studies for further details.

Risk of bias in included studies

The methodological quality in general was satisfactory. The assessment of bias in the included studies has been set out in the 'Risk of bias' tables following the Characteristics of included studies tables and summarised in Figure 1 and Figure 2.

Figure 1. 'Risk of bias' graph: review authors' judgements about each risk of bias item presented as percentages across all included studies.

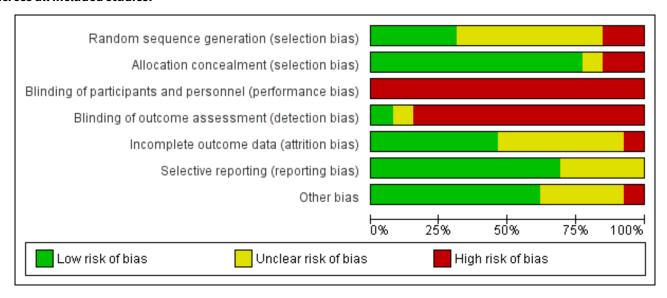
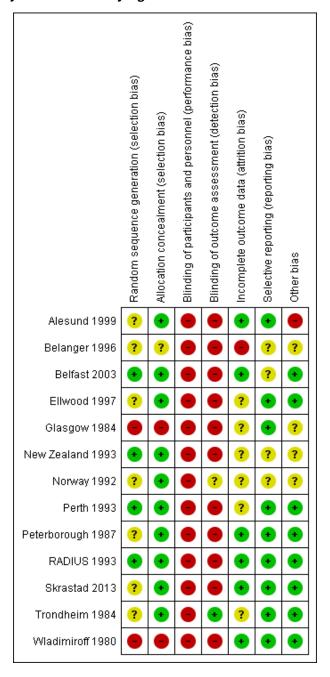




Figure 2. 'Risk of bias' summary: review authors' judgements about each risk of bias item for each included study.



Allocation

Of the 13 included trials, four adequately reported on the method of randomisation. Seven of the trials were unclear in relation to selection bias; in all of these studies the process of randomisation was either not described or not adequately described. Two of the studies were assessed as having a high risk of selection bias as these were both pseudo-randomised by hospital number (Glasgow 1984 (UK); Wladimiroff 1980 (The Netherlands)).

Regarding allocation concealment 10 of the 13 trials were assessed to have a low risk of this component of selection bias. One trial of unclear risk did not describe the technique used (Belanger 1996), and two trials at high risk of bias used pseudo-randomised

by hospital number (Glasgow 1984 (UK); Wladimiroff 1980 (The Netherlands)).

Blinding

Blinding was not possible due to the interventions used in the included trials. Only the Trondheim 1984 trial managed to include some form of blinding of outcome assessment and even then only for neonatal outcomes. Norway 1992 was judged to have unclear risk of bias in this domain. All other studies were assessed to be at high risk of performance and detection bias.



Incomplete outcome data

Six of the trials were assessed to have a low risk of attrition bias. There was unclear attrition bias in six trials, as there was insufficient information in two of these trials (Ellwood 1997; New Zealand 1993) and in the other four there was a loss of follow-up of unclear significance (Glasgow 1984; Norway 1992; Perth 1993; Trondheim 1984). The Belanger 1996 trial was assessed as high risk of attrition bias as it did not state the size of the full sample.

Selective reporting

Nine of the 13 trials were considered to have a low risk of reporting bias. The four remaining trials were assessed to be of unclear risk. In all four, this was due to a lack of detail to make a definitive decision (Belanger 1996; Belfast 2003; New Zealand 1993; Norway 1992).

Other potential sources of bias

Eight of the 13 studies were assessed to be of low risk of other forms of bias. Four studies were unclear, in three of these it was due to a lack of information provided (Belanger 1996; New Zealand 1993; Norway 1992), whilst in the Glasgow 1984 paper there were more participants from social class 'V' in the reported group, the significance of which was unclear. The Alesund 1999 trial was considered a high risk of other bias as there were more smokers in the screened group.

Effects of interventions

See: Summary of findings for the main comparison Routine ultrasound > 24 weeks for pregnant women

Routine ultrasound greater than 24 weeks versus no/ concealed/selected ultrasound greater than 24 weeks

Primary outcomes

There was no significant effect of ultrasound after 24 weeks on the outcomes of induction of labour (average risk ratio (RR) 0.93, 95% confidence interval (CI) 0.81 to 1.07, six studies; 22,663 women; Analysis 1.1; random-effects analysis, Heterogeneity: Tau² = 0.02; Chi^2 = 23.07, (P = 0.0003); I^2 = 78%, evidence graded as moderate quality) or caesarean section (average RR 1.03, 95% CI 0.92 to 1.15; six studies; 27,461 women; Analysis 1.2; random-effects analysis, Heterogeneity: $Chi^2 = 10.79$, (P = 0.06); $I^2 = 54\%$, evidence graded as high quality). There was substantial heterogeneity for both of these outcomes. For the outcome of induction of labour, removing Alesund 1999 reduced the heterogeneity to 10%; the effect size changed minimally and remained statistically insignificant. For the outcome of caesarean section, removal of Trondheim 1984 had little effect on heterogeneity or on the overall effect estimate. Both Alesund 1999 and Trondheim 1984 collected data between 1979 and 1981, when ultrasound practices may have differed substantially and ultrasound technology was less advanced compared with later trials in this review. No group differences were detected for the remaining primary outcomes: preterm delivery before 37 weeks (RR 0.96, 95% CI 0.85 to 1.08; two studies, 17,151 women; Analysis 1.4, evidence graded as high quality) and perinatal mortality (RR 1.01, 95% CI 0.67 to 1.54; eight studies; 30,675 infants; Analysis 1.3, evidence graded as moderate quality). Data were not available for the outcomes of preterm delivery less than 34 weeks, neurodevelopment at age two or maternal psychological effects.

Secondary outcomes

There were a number of secondary outcomes captured. Specifically, ultrasound after 24 weeks had no effect on antenatal admission (average RR 1.07, 95% CI 0.80 to 1.43; four studies; 5396 women; Analysis 1.5; random-effects analysis, Heterogeneity: $Tau^2 = 0.07$; $Chi^2 = 19.63$, (P = 0.0002); $I^2 = 85\%$). There was considerable heterogeneity for this outcome. Two studies reported on whether routine ultrasound increased or reduced the need for further ultrasound scans. The findings from the two studies were not consistent, therefore we have not pooled results; in the New Zealand 1993 trial, women who had routine scans were less likely to need further scans (RR 0.63, 95% CI 0.53 to 0.76, 1527 women), conversely, in the Trondheim 1984 study, women in the routine scan group had an increased risk of undergoing further scans although the difference between groups was not statistically significant (RR 1.34, 95% CI 0.95 to 1.89, 1009 women). (Analysis 1.8).

There were no group differences found for the following labour and delivery outcomes: number of days in hospital (mean difference (MD) 0.10, 95% CI 0.07 to 0.13; one study; 877 women; Analysis 1.6); cardiotocograph (CTG) (RR 1.02, 95% CI 0.97 to 1.06; one study; 2000 women; Analysis 1.7); instrumental delivery (RR 1.05, 95% CI 0.95 to 1.16; five studies; 12,310 women; Analysis 1.9); elective caesarean section (RR 1.09, 95% CI 0.89 to 1.34; four studies; 5884 women; Analysis 1.10); or emergency caesarean section (RR 1.03, 95% CI 0.89 to 1.20; five studies; 12,310 women; Analysis 1.11).

Significantly less women who had ultrasound after 24 weeks gave birth to post-term infants, with delivery after 42 weeks' gestation (RR 0.69, 95% CI 0.59 to 0.81; two studies; 17,151 women; Analysis 1.25).

There were no treatment group differences in the gestational age of infants at delivery (MD -0.10, 95% CI -0.22 to -0.02; three studies; 9303 infants; fixed-effect analysis, Heterogeneity: $\text{Chi}^2 = 5.36$, (P = 0.07); $\text{I}^2 = 63\%$, Analysis 1.12). Random-effects analysis had no impact on the high heterogeneity for this outcome. Neither did ultrasound have an effect on birthweight outcomes: birthweight (MD 4.40, 95% CI -8.89 to 17.69; five studies; 26,136 infants; Analysis 1.13); birthweight less than the 10th centile (average RR 0.98, 95% CI 0.74 to 1.28; four studies; 20,293 infants; random-effects analysis, Heterogeneity: $\text{Tau}^2 = 0.05$; $\text{Chi}^2 = 10.15$, (P = 0.02); $\text{I}^2 = 70\%$, Analysis 1.14); birthweight less than the 5th centile (RR 1.18, 95% CI 0.81 to 1.74; two studies; 2404 infants; Analysis 1.26); and low birthweight less than 2.5 kg (RR 0.92, 95% CI 0.71 to 1.18; three studies; 4510 infants; Analysis 1.15).

Routine ultrasound after 24 weeks also had no significant effect on the following neonatal outcomes: neonatal resuscitation (RR 0.95, 95% CI 0.84 to 1.08; five studies; 12,909 infants, Analysis 1.16); neonatal ventilation (average RR 0.64, 95% CI 0.23 to 1.77; two studies; 3004 infants; random-effects analysis, Heterogeneity: Tau² = 0.42; Chi² = 3.92, (P = 0.05); I² = 74%, Analysis 1.17); Apgar score of less than seven at five minutes (average RR 0.89, 95% CI 0.41 to 1.93; four studies; 5889 infants; random-effects analysis, Heterogeneity: Tau² = 0.35; Chi² = 7.39, (P = 0.06); I² = 59%, Analysis 1.19); admission to special care baby unit (RR 1.01, 95% CI 0.91 to 1.14; five studies; 12,915 infants; Analysis 1.18); or stillbirths (RR 1.18, 95% CI 0.51 to 2.70; six studies; 28,107 infants; Analysis 1.20).

Composite neonatal outcomes and neonatal outcomes omitting congenital abnormalities also detected no group differences:



moderate neonatal morbidity (RR 0.97, 95% CI 0.81 to 1.16; one study; 15,281 infants; Analysis 1.27); severe neonatal morbidity (RR 1.03, 95% CI 0.78 to 1.36; one study; 15,281 infants; Analysis 1.28); perinatal mortality excluding congenital abnormalities (average RR 1.13, 95% CI 0.58 to 2.19; six studies; 28,133 infants; random-effects analysis, Heterogeneity: $Tau^2 = 0.27$; $Chi^2 = 8.26$, (P = 0.08); $I^2 = 52\%$, Analysis 1.22); stillbirths excluding congenital abnormalities (RR 0.05, 95% CI 0.00 to 0.90; two studies; 2902 infants; Analysis 1.23); neonatal deaths excluding congenital abnormalities (RR 1.99, 95% CI 0.18 to 21.96; two studies; 2901 infants; Analysis 1.24).

Finally, three studies with 314 women reported no group differences for perinatal mortality in twin pregnancies (RR 0.63, 95% CI 0.24 to 1.66; Analysis 1.29).

Subgroup analyses were not performed due to the small number of included studies and limited data. For a number of the comparisons there was considerable heterogeneity. Where heterogeneity was substantial (over 50%), we have used a random-effects model. In view of high levels of heterogeneity these results should be interpreted with caution. Possible causes of heterogeneity include the wide variation in ultrasound practice during the dates of the included trials (1979 to 2013). Protocol surrounding ultrasound practice will have changed; also, ultrasound technology has advanced rapidly over this time period. There may also be important differences in women receiving ultrasound across this time period. Finally, baseline rates of important birth outcomes like caesarean section will also have changed markedly since 1979.

Serial ultrasound and Doppler ultrasound versus selective ultrasound

Only Perth 1993 and Ellwood 1997 compared serial ultrasound and Doppler ultrasound against selective ultrasound. However, because only Perth 1993 provided usable data, the findings here reflect this one study with 2834 women, with the exception of Analysis 2.15, which shows data from both trials.

Primary outcomes

There was no benefit of serial ultrasound and Doppler ultrasound compared to selective ultrasound after 24 weeks in relation to induction of labour (RR 1.02, 95% CI 0.92 to 1.14; Analysis 2.1) and caesarean section (RR 0.89, 95% CI 0.76 to 1.03; Analysis 2.2). There was also no benefit in relation to perinatal mortality (RR 0.59, 95% CI 0.30 to 1.17; Analysis 2.3). There were no data available for preterm delivery, either less than 34 weeks or less than 37 weeks, neurodevelopment at age two or maternal psychological effects.

Secondary outcomes

There were a range of secondary outcomes captured, and for the most part there was no evidence of a benefit of serial ultrasound and Doppler ultrasound after 24 weeks compared to selective ultrasound.

There were no group differences for the following labour and delivery outcomes: CTG (RR 1.01, 95% CI 0.93 to 1.09; Analysis 2.4); elective caesarean section (RR 0.95, 95% CI 0.77 to 1.17; Analysis 2.5); emergency caesarean section (RR 0.82, 95% CI 0.64 to 1.05; Analysis 2.6).

Serial and Doppler ultrasound had no effect on the following neonatal outcomes: gestational age at delivery (MD -0.10, 95% CI -1.21 to 1.01; Analysis 2.7); neonatal resuscitation (RR 0.98, 95%

CI 0.92 to 1.05; Analysis 2.13); neonatal ventilation (RR 0.67, 95% CI 0.41 to 1.09; Analysis 2.14); Apgar score less than seven at five minutes (RR 0.77, 95% CI 0.46 to 1.27; Analysis 2.16); or admission to special care baby unit (RR 0.95, 95% CI 0.69 to 1.30; two studies; 2979 infants; Analysis 2.15).

Most birthweight outcomes also showed no advantage for serial and Doppler ultrasound, including birthweight (MD -25.00, 95% CI -67.53 to 17.53; Analysis 2.8); low birthweight less than 2.5 kg (RR 1.14, 95% CI 0.85 to 1.52; Analysis 2.11); and very low birthweight less than 1.5 kg (RR 1.27, 95% CI 0.65 to 2.49; Analysis 2.12). Two exceptions showing statistically significant differences were birthweight less than the 10th centile (RR 1.36, 95% CI 1.10 to 1.68; Analysis 2.9) and birthweight less than the 3rd centile (RR 1.66, 95% CI 1.10 to 2.51; Analysis 2.10). Lower birthweight occurred more frequently in the treatment groups for these outcomes. Metanalysis was not possible as data came from only one study.

Sensitivity analysis

One of the trials examining ultrasound after 24 weeks' gestation used a quasi-randomised design with poor allocation concealment (Glasgow 1984). We conducted a sensitivity analysis, removing this trial from each primary outcome where it contributed data, to see if this would make any difference to the direction of findings or to the size of the treatment effect. Removing this study made little difference to the results; it did not change the direction of findings and, as it was a relatively small study, made little difference to the size of the treatment effect even for those outcomes where only a small number of trials contributed data.

DISCUSSION

Summary of main results

Meta-analysis of the data shows very little difference between groups in antenatal, obstetric and neonatal outcomes, apart from less women giving birth post-term if they had ultrasound after 24 weeks. Data from two trials were available for the outcome post-term birth (Peterborough 1987; RADIUS 1993), with the latter contributing 98.9% of the data. In the RADIUS trial, women in the control group did not have routine early pregnancy ultrasound but women in the intervention group did, and therefore gestational dating was not accurate for the control group, hence it is difficult to know if the pregnancies in the control group were indeed postterm or not, or if there may have been more or less post-term pregnancies. Given this, we are not able to conclude anything about the finding of less post-term births in the intervention group. As current clinical practice is to offer induction of labour before 42 completed weeks' gestation in pregnancy, it is unlikely that this issue will ever be resolved.

Overall, perinatal mortality was no different for all fetuses or neonates, and twin pregnancies. Although there was some heterogeneity in perinatal mortality overall ($I^2 = 29\%$), there was increased heterogeneity in perinatal mortality corrected for abnormality ($I^2 = 52\%$). This was due to the Peterborough 1987 (UK) trial data that suggested a significant reduction in the number of congenitally normal stillbirths. This trial was unique in that it was an evaluation of placental grading as an adjunct to routine late pregnancy ultrasound. The authors state that this observation was not a formal prior hypothesis and may be an overestimate of the true effect of the test. In view of the nature of the trial, i.e.



single centre and limited power to assess perinatal outcome (2000 participants), and the fact that it was performed over two decades ago (1987), this finding needs to be revisited in future research.

There was no overall difference in the incidence of babies being small-for-gestational age (SGA) at birth (less than 10th percentile) comparing experimental and control groups (average risk ratio 0.98, 95% confidence interval 0.74 to 1.28), but there was high heterogeneity ($I^2 = 70\%$), mainly due to the findings of the Belfast 2003 study which found fewer babies less than 10th birthweight centile in the intervention group. It is difficult to interpret this finding as it cannot be attributable to late ultrasound scan because ultrasound itself cannot promote fetal growth. Whilst, theoretically, there is some potential scope to decrease the impact of low birthweight by recognition of fetal growth restriction through ultrasound screening, and early planned delivery, there is no evidence to suggest that ultrasound late in pregnancy has any specific beneficial effect.

Overall completeness and applicability of evidence

The ultrasound scan protocols in each trial varied. It is difficult to assess the effect of scans before 24 weeks' gestation on the outcome measures. For example, the finding of a reduction in post-term delivery in the screened group of the RADIUS 1993 (USA) study is probably due to better gestational age assessment at the 18 to 20 week scan. In addition, the reason for routine ultrasound scan after 24 weeks' gestation differed amongst trials. Ideally, subgroup analyses according to the reason for the scan would resolve the possible difference in outcomes according to the diagnostic approach, but there are not enough studies to perform meaningful subgroup analyses. This may explain some of the heterogeneity and the results of the meta-analysis should be viewed in this light.

Furthermore, ultrasound is a diagnostic tool, and on its own would not be expected to improve outcomes unless if it is abnormal it leads to a change in management. While the presumption is that the ultrasound findings were evaluated by clinicians and action taken accordingly, none of the trials had management algorithms that should have been followed on the basis of the ultrasound findings and therefore management was not standardised. The finding of no effect on outcomes needs to be considered in this context.

To target the effect of late pregnancy, ultrasound trials should ideally compare ultrasound in late pregnancy alone versus no ultrasound or similar control, however this is generally not how these studies have been designed. Commonly, the influence of first and second trimester ultrasounds is difficult to disentangle. Also, the fact that assessment of most parameters at late pregnancy ultrasound are based on gestational reference data, which in turn rely on accurate gestational dating in early pregnancy, further compounds this issue. Therefore, it is neither realistic, nor pragmatic, to consider ultrasound in late pregnancy in isolation.

Only one of the trials was powered to address perinatal mortality, RADIUS 1993, which randomised over 15,000 women. It was also the only trial with extractable data whereby women in the control group did not have at least one routine scan as it was mainly designed to evaluate detection of fetal abnormalities with routine ultrasound. This trial was undertaken between 1987 and 1991 and its findings may not be relevant in today's developed-world maternity setting given the relatively rapid advances in ultrasound

technology and the fact that almost all women have routine ultrasound at earlier gestations, that is, the first and second trimesters.

Apart from the Belfast 2003 trial, trials were undertaken over a period of time from early introduction into clinical practice to widespread use and assimilation during which biometric formulae, technology and techniques, parameters of normality and deviation from normal and consensus about how to assess fetal size and well being ultrasonographically were still being debated. Some of the findings inevitably therefore have a shelf life. The Belfast 2003 trial more reflects the ultrasonographic approach to assessing fetal growth and well being by today's standards even though it was published 11 years ago, but it showed no benefit in terms of perinatal outcome apart from fewer babies less than 10th birthweight centile in the ultrasound group but as previously mentioned this cannot be attributable to scan as ultrasound cannot promote better growth.

In the Perth 1993 (Australia) trial there was an unexpected finding of significantly higher intrauterine growth restriction in the serial ultrasound and Doppler examination group (i.e. the intensive group). The authors state that while this may have been a chance finding, it is possible that frequent exposure to ultrasound may have influenced fetal growth. This finding was not associated with increased perinatal morbidity and mortality, and follow-up of these children at one year of age found that the difference was no longer discernible (Newnham 1996). The authors stress the need for further investigation of the effects of frequent ultrasound exposure on fetal growth. Furthermore, if this were a true effect, the modality responsible (Doppler ultrasound versus real-time ultrasound) would need to be elucidated. More recent data from this trial reporting findings for children at eight years of age found no negative effect associated with serial ultrasound in terms of physical size or speech, language and neurological development (Newnham 2004).

Long-term follow-up of children from the Norwegian studies revealed no positive or negative effects of exposure to ultrasound in children aged eight to nine years although there was an association between exposure to ultrasound in utero and non-right handedness. This finding may be a chance one, but merits further investigation (Alesund 1999; Norway 1992; Trondheim 1984). A recent follow-up study of young adults born to women recruited for Perth 1993 shows no links between the timing and frequency of ultrasound with a diagnosis of Autism Spectrum Disorder or the presence of autistic-like traits (Stoch 2012).

The RADIUS 1993 (USA) trial and Skrastad 2013 trial were the only studies that addressed detection of fetal anomalies in the third trimester. The overall fetal anomaly detection rate in the RADIUS 1993 trial was poor, at 35%. After 24 weeks' gestation, 34/156 (22%) anomalous fetuses were detected in the screened group, and 10/155 (6.5%) anomalies were detected in the control group. The overall fetal anomaly detection rate in the Skrastad 2013 trial was 56%. After 23 weeks' gestation, 25/70 (36%) anomalies were detected in the screened group, and 17/83 (20%) anomalies were detected in the control group. However, the better detection rate in the screened groups in both trials did not translate into an improvement in infant survival.

Few of the trials addressed long-term neurodevelopmental outcome and none examined maternal psychological outcome,



and it is arguable that these are the most important outcomes. The Belanger 1996 trial reported results of Bayley evaluations at six and 18 months on a subset of 286 infants in the study and found no difference in the Mental Development Index and Psychomotor Development Index in those in the intervention group compared with those in the control group. Exposure of the expectant mother to uncertainty and possible anxiety about the health of her baby has implications which may be far reaching. In addition, perinatal survival does not automatically translate into long-term success, as little is known about the long-term prognosis of the in utero compromised fetus.

Quality of the evidence

Overall, risk of bias in these studies was mixed. Broadly, for most of the included studies risk of bias was assessed as low for allocation concealment and selective reporting, unclear for random sequence generation and incomplete outcome data and high for blinding of both outcome assessment and participants and personnel. For the primary outcomes, GRADE assessments are shown in the Summary of findings for the main comparison. Perinatal mortality was considered to be of moderate quality; the evidence for this outcome was downgraded for a wide confidence interval crossing the line of no effect. Preterm birth less than 37 weeks was graded as of high quality, as was the outcome of caesarean section. The outcome of induction of labour was graded as of moderate quality due to the high heterogeneity for this outcome (78%). Three outcomes considered important to this review were not measured in any of the included trials and therefore have no quality rating from GRADE: preterm birth less than 34 weeks, maternal psychological effects and neurological development at age two.

Potential biases in the review process

The review closely followed the Cochrane Group guidance which reduces the risk of bias in the process. It is noteworthy that this current update has featured a significant change to the previous authorship group which may affect how bias itself is appraised.

Agreements and disagreements with other studies or reviews

There are no other directly comparable systematic reviews. The findings of this review did not contradict those of the Cochrane review on the effects of ultrasound in early pregnancy (Whitworth 2010).

AUTHORS' CONCLUSIONS

Implications for practice

There is no evidence that routine ultrasound in late pregnancy improves perinatal outcome. As a result of this review, it is not clear what aspects of late pregnancy ultrasound may be valuable in centres where it is undertaken. However, placental grading may be useful, and perhaps should be considered in late pregnancy ultrasound, whether routine or selective.

Implications for research

There is a lack of data about the potential psychological effects of routine ultrasound in late pregnancy, and the effects on both short-and long-term neonatal and childhood outcomes. Future studies should address these issues.

Based on the available data about the value of placental grading, future research of late pregnancy ultrasound should include assessment of placental texture.

Future trials should include management algorithms in order to assess the impact of acting upon abnormal ultrasound findings.

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CHARACTERISTICS OF STUDIES

Characteristics of included studies [ordered by study ID]

Alesund 1999

Methods	Randomisation by sealed envelopes.
Participants	Nearly all women in that geographical area, including those with 'high-risk' pregnancies. Recruitment 1979-1981. 1628 women.
Interventions	Routine ultrasound examination at 18 weeks (biparietal diameter measured) and 32 weeks (biparietal diameter and mean abdominal diameter) with additional examination at 36 weeks' gestation if fetus SGA and/or presenting by breech - versus selective examination for clinical indications only.

^{*} Indicates the major publication for the study



Alesund 1999 (Continued)			
Outcomes	Obstetric interventions (antepartum and intrapartum) for singleton pregnancies only. Perinatal outcome indices for all pregnancies (including multiple pregnancies).		
Notes	This trial was reported in letter form only in 1984. It subsequently became clear that there were inconsistencies in results, and the data were subsequently re-analysed. The data entered in this review are derived from more recent unpublished and published reports.		
Risk of bias			
Bias	Authors' judgement	Support for judgement	
Random sequence generation (selection bias)	Unclear risk	Not stated.	
Allocation concealment (selection bias)	Low risk	Described as "sealed envelope".	
Blinding of participants and personnel (perfor- mance bias) All outcomes	High risk	Not feasible.	
Blinding of outcome assessment (detection bias) All outcomes	High risk	Not feasible.	
Incomplete outcome data (attrition bias) All outcomes	Low risk	The data could be re-included.	
Selective reporting (reporting bias)	Low risk	Selective outcome reporting bias not apparent.	
Other bias	High risk	More smokers in screened group; historical study.	
Belanger 1996			
Methods	Randomised controlled	d trial. Does not describe method of randomisation.	
Participants	Total number of women randomised not stated. Follow-up data for 286 singleton infants born to mothers.		
Interventions	Intervention group: ultrasound at 16 to 20 weeks and 30 to 36 weeks, comparison group: scans only when clinically indicated.		
Outcomes	Bayley evaluations – Mental Development Index (MDI) and Psychomotor Developmental (PDI).		
Notes	Brief abstract, lacks full details for inclusions, data available not relevant.		

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Does not give sufficient detail; study described only as randomised.



Belanger 1996 (Continued) Allocation concealment	Unclear risk	Allocation concealment is not described.
(selection bias)	Unctearrisk	Allocation concealment is not described.
Blinding of participants and personnel (perfor- mance bias) All outcomes	High risk	Not feasible.
Blinding of outcome assessment (detection bias) All outcomes	High risk	Does not give sufficient detail. Outcomes were collected at 6 and 18 months, with blinding not stated.
Incomplete outcome data (attrition bias) All outcomes	High risk	Authors do not state the size of the full sample. Data here represent a subset.
Selective reporting (reporting bias)	Unclear risk	Data for 2 pre-specified neurological development outcomes were collected for this subset of infants. It is unclear whether additional outcomes for the full sample were collected.
Other bias	Unclear risk	Bias assessment significantly compromised by lack of detail.

Belfast 2003

Methods	Randomised controlled trial. Randomisation by sealed, numbered envelopes.
Participants	Women recruited at 30 weeks' gestation assessed as low risk with singleton pregnancy and dates confirmed by 18-20 weeks' anomaly scan.
	Exclusion criteria: known medical or obstetric problems or known fetal anomaly.
	1998 women recruited over a 21-month period.
Interventions	Assessment 30 to 32 weeks and at 36 to 37 weeks by a midwife as part of routine care with midwife estimate of fetal size, presentation, position and amniotic fluid volume. In addition, the study group had ultrasound examinations by the specially trained midwife to assess liquor volume, fetal weight and placental maturity. The comparison group had selective ultrasound examinations if indicated.
Outcomes	SGA at birth, admission to special care and antenatal interventions.
Notes	

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Computer-generated (restricted to achieve group balance).
Allocation concealment (selection bias)	Low risk	Sealed, numbered envelopes.
Blinding of participants and personnel (perfor- mance bias) All outcomes	High risk	Not feasible.



Belfast 2003 (Continued)		
Blinding of outcome assessment (detection bias) All outcomes	High risk	Not feasible.
Incomplete outcome data (attrition bias) All outcomes	Low risk	Good follow-up for most outcomes.
Selective reporting (reporting bias)	Unclear risk	Difficult to interpret the results relating to the main outcome.
Other bias	Low risk	None detected.

Ellwood 1997

Methods	Randomised controlled trial.	
Participants	Pregnant women < 20 weeks' gestation, recruited at booking visit to antenatal clinic. Women must have no pre-existing medical conditions and in first ongoing pregnancy (1 first trimester loss allowed). 364 women recruited; interim report of data for 145 women.	
Interventions	Intervention group: routine 18 to 20-week scan, followed by uterine artery Doppler at 24 to 26 weeks; transvaginal assessment of cervix 24 to 26 weeks; growth and amniotic fluid index at 38 weeks. Comparison group: routine 18 to 20-week scan and any others clinically indicated.	
Outcomes	Gestation age at delivery, preterm delivery, unplanned admissions for pre-eclampsia or intrauterine growth restriction and length of maternal stay, Apgar < 7 at 5 minutes, neonatal intensive care unit admissions and length of neonatal intensive care unit stay.	

Notes

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Sequence generation not described.
Allocation concealment (selection bias)	Low risk	Quote: "Randomisation carried out using the sealed envelope technique".
Blinding of participants and personnel (perfor- mance bias) All outcomes	High risk	Not feasible.
Blinding of outcome assessment (detection bias) All outcomes	High risk	Not feasible.
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	364 women recruited; interim report of data for 145 women. 2 women miscarried, 3 withdrew and 1 lost to follow-up.



Ellwood 1997 (Continued)		
Selective reporting (reporting bias)	Low risk	Prespecified outcomes have been reported.
Other bias	Low risk	None detected.

Glasgow 1984

Methods	Pseudo-randomisation according to last digit in hospital number.	
Participants	877 women attending the hospital antenatal clinic between 34 to 36.5 weeks' gestation with uncomplicated singleton pregnancies, i.e. low-risk pregnancies.	
Interventions	All women had an ultrasound examination < 24 weeks' gestation for gestational dating. All had further ultrasound scan at 34 to 36.5 weeks' gestation to measure crown rump length and trunk area, but in the study group the 2 measurements were multiplied and the results plotted and reported in the case notes (i.e. revealed). Further management was the responsibility of the clinical staff. No requests for control group measurements to be revealed occurred, but this option was available to clinicians.	
Outcomes	Obstetric interventions (antepartum and intrapartum) and perinatal outcome indices.	
Notes	This study addressed ultrasound screening for small for dates.	
Risk of bias		

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	High risk	Described as allocated "from their hospital index numbers".
Allocation concealment (selection bias)	High risk	See above.
Blinding of participants and personnel (perfor- mance bias) All outcomes	High risk	Not feasible.
Blinding of outcome assessment (detection bias) All outcomes	High risk	Not feasible.
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Small loss to follow-up.
Selective reporting (reporting bias)	Low risk	Selective outcome reporting not detected.
Other bias	Unclear risk	There were more participants from social class V in the reported group.



New Zealand 1993				
Methods	Randomised by womer random 1 or 2 and a str	n selecting 1 of a number of envelopes (< 6) containing a computer-generated udy number.		
Participants		ho attended antenatal clinic < 24 weeks' gestation, i.e. unselected population. xcluded once diagnosed (and study numbers reused). 1527 women.		
Interventions	weeks' gestation (ideal weight fell below the 2	All women had a dating scan 16 to 24 weeks' gestation. Study group had a further scan at 32 to 36 weeks' gestation (ideally 34 weeks' gestation) that aimed to detect SGA fetuses, and if estimated fetal weight fell below the 20th centile for gestation, this was reported and additional scans recommended but not arranged. Clinicians were able to order further scans for the control group if clinically indicated.		
Outcomes	Mainly perinatal outco	me indices. Number of further ultrasound scans.		
Notes	Scan to detect SGA.			
Risk of bias				
Bias	Authors' judgement	Support for judgement		
Random sequence generation (selection bias)	Low risk	Sequence computer-generated.		
Allocation concealment (selection bias)	Low risk	Randomised by women selecting 1 of a number of envelopes (< 6) containing a computer-generated random 1 or 2 and a study number.		
Blinding of participants and personnel (perfor- mance bias) All outcomes	High risk	Not feasible.		
Blinding of outcome as- sessment (detection bias) All outcomes	High risk	Not feasible.		
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Not stated.		
Selective reporting (reporting bias)	Unclear risk	No information provided.		
Other bias	Unclear risk	No information provided.		

Norway 1992

Methods	Combined findings from the Tronheim and Alesund trials for childhood developmental outcomes.	
Participants	Alesund - nearly all women in that geographical area, including those with 'high-risk' pregnancies. Recruitment 1979-1981. 1628 women.	
	Trondheim - 1009 pregnant women in Trondheim attending for antenatal care between 1979-1980.	
Interventions	Alesund - routine ultrasound examination at 18 weeks (biparietal diameter measured) and 32 weeks (biparietal diameter and mean abdominal diameter) with additional examination at 36 weeks' gestation if fetus SGA and/or presenting by breech - versus selective examination for clinical indications only.	



Norway 1992 (Continued)	Trondheim - study grou	up offered ultrasound examinations at 19 weeks' and 32 weeks' gestation.		
Outcomes	Follow-up of singletons at 8 to 9 years including teacher assessed school performance, along with assessments of reading, speech and intelligence scores.			
Notes		This is not strictly a separate study, but findings from the Alesund and Trondheim trials were combined for long-term follow-up.		
Risk of bias				
Bias	Authors' judgement	Support for judgement		
Random sequence generation (selection bias)	Unclear risk	Not stated (both studies).		
Allocation concealment (selection bias)	Low risk	Sealed envelopes.		
Blinding of participants and personnel (perfor- mance bias) All outcomes	High risk	Not feasible.		
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Not stated.		
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	2011 of 2824 eligible followed up.		
Selective reporting (reporting bias)	Unclear risk	Outcome data collected are reported.		
Other bias	Unclear risk	These data are for long-term follow-up.		

Perth 1993

Methods	Sealed envelopes.	
Participants	2834 singleton pregnancies. Criteria for recruitment were gestational age 16 to 20 weeks, sufficient proficiency in English, expected to deliver at the hospital and an intention to remain in Western Australia so that childhood follow-up would be feasible.	
Interventions	The 'regular' group had an ultrasound examination at 18 weeks for fetal biometry, subjective amniotic fluid assessment and placental morphology and location, and any further scans in pregnancy were conducted on clinicians request. The 'intensive group' had the aforementioned ultrasound examination, plus an amniotic fluid index and continuous wave Doppler ultrasound of the umbilical artery and an arcuate artery within the placental vascular bed at 18, 24, 28, 34 and 38 weeks' gestation. The Doppler ultrasound parameter reported was systolic/diastolic ratio. Results of these examinations were recorded in the hospital chart, but no clinical management guidance was given.	
Outcomes	Obstetric interventions (antepartum and intrapartum) and perinatal outcome indices.	
Notes	The published study reports the results overall, but little data are available for extraction. The authors were contacted and provided unpublished data.	



Perth 1993 (Continued)

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Described as "computer-generated random numbers".
Allocation concealment (selection bias)	Low risk	Described as "sealed envelopes".
Blinding of participants and personnel (perfor- mance bias) All outcomes	High risk	Not feasible.
Blinding of outcome assessment (detection bias) All outcomes	High risk	Not feasible.
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Some loss to follow-up in both groups. "13 were lost to follow up in the intensive group of the trial and 20 in the regular" care group.
Selective reporting (reporting bias)	Low risk	Selective outcome reporting bias not detected.
Other bias	Low risk	Other bias not detected.

Peterborough 1987

Methods	Randomisation by opaque sealed envelopes.	
Participants	2000 pregnant women attending the ultrasound department for routine third trimester scans, including multiple pregnancies.	
Interventions	All women were offered routine early pregnancy ultrasound and 2 routine scans in the third trimester. Placental grading was performed at the routine third trimester scan. The results of placental grading in the study group were revealed, and the control group concealed. Clinical management in both groups was left entirely to the clinician responsible for care.	
Outcomes	Obstetric interventions (antepartum and intrapartum) and perinatal outcome indices.	
Notes	This study addresses the value of placental grading at routine third trimester ultrasound.	
Risk of bias		

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Described as "randomly allocated to 1 of 2 groups".
Allocation concealment (selection bias)	Low risk	Described as "a correspondingly numbered, sealed, opaque envelope".



Peterborough 1987 (Continued,)	
Blinding of participants and personnel (perfor- mance bias) All outcomes	High risk	Not feasible.
Blinding of outcome assessment (detection bias) All outcomes	High risk	Not feasible.
Incomplete outcome data (attrition bias) All outcomes	Low risk	No losses to follow-up.
Selective reporting (reporting bias)	Low risk	Selective outcome reporting not detected.
Other bias	Low risk	No other bias apparent.

RADIUS 1993

Methods	Randomisation by microcomputer after stratification by practice site. 109 participating practice sites recruited low-risk women. Ultrasounds took place in 1 of 28 participating sites. Intention-to-treat.
Participants	15151 pregnant women who did not have "an indication for ultrasonography" based on uncertain gestational age, previous or index pregnancy complication, medical disorder. Therefore, those eligible were at low risk of adverse pregnancy outcome, and comprised 40% of the total population.
Interventions	Ultrasound screen at 18 to 20 weeks' and 31 to 33 weeks' gestation, versus selective ultrasonography only.
Outcomes	Perinatal outcome indices. The primary outcomes were perinatal mortality and moderate/severe neonatal morbidity.
Notes	

RISK OI DIUS		
Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Described as "computer-generated randomisation sequence".
Allocation concealment (selection bias)	Low risk	Central randomisation performed after stratification by practice site.
Blinding of participants and personnel (perfor- mance bias) All outcomes	High risk	Not feasible.
Blinding of outcome assessment (detection bias) All outcomes	High risk	Not feasible.



RADIUS 1993 (Continued)		
Incomplete outcome data (attrition bias) All outcomes	Low risk	15,530 women recruited. Data for 15,151; 252 women (1.6%) lost to follow-up and 127 women (0.8%) had spontaneous miscarriage. Reasons for loss similar for 2 groups.
Selective reporting (reporting bias)	Low risk	Selective outcome reporting bias not detected.

Skrastad 2013

Methods	Randomised controlled trial. All pregnant women attending routine prenatal care living in 9 municipalities including and surrounding Trondheim, Norway. Data were collected between November 1989 and August 1992. The trial was not previously published "because the initial principal investigator left the department in the 1990s".	
Participants		
Interventions	Routine ultrasound at 18 and 33 weeks versus routine ultrasound at 18 weeks and on clinical indication only.	
Outcomes	Detection rates of SGA and LGA babies, congenital anomalies, other adverse perinatal outcomes including caesarean section and ELCS, induction of labour, operative delivery, birthweight, perinatal death (stillbirth, neonatal death, perinatal death with no anomalies), Apgar < 7 at 5 minutes, meconium-stained fluid, resuscitation, and admission to neonatal intensive care unit.	

Notes

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Sequence generation not described. Study described as randomised.
Allocation concealment (selection bias)	Low risk	Sealed envelope method used.
Blinding of participants and personnel (perfor- mance bias) All outcomes	High risk	Not feasible.
Blinding of outcome as- sessment (detection bias) All outcomes	High risk	Not feasible.
Incomplete outcome data (attrition bias) All outcomes	Low risk	42 women for whom estimated date of delivery was not available were excluded from the contributing data for the outcomes of SGA and LGA; these women were included in other outcomes. Study flowchart published with clear reasons for attrition. Loss to follow-up 3.5% in study arm and 4.25% in control arm. Intention-to-treat analysis otherwise undertaken.
Selective reporting (reporting bias)	Low risk	Prespecified outcomes are reported.



Skrastad 2013 (Continued)

Other bias Low risk None found.

Trondheim 1984

Methods	Randomised by sealed-envelope method.	
Participants	1009 pregnant women in Trondheim attending for antenatal care between 1979-1980.	
Interventions	Study group offered ultrasound examinations at 19 weeks' and 32 weeks' gestation.	
Outcomes	Obstetric interventions (antepartum and intrapartum) and perinatal outcome indices.	
Notes	Some data only presented for singletons (mean birthweight, birthweight < 10th centile, low birthweight, neonatal resuscitation, admission to special care, Apgar scores).	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Not stated.
Allocation concealment (selection bias)	Low risk	Described as sealed envelopes.
Blinding of participants and personnel (perfor- mance bias) All outcomes	High risk	Not feasible.
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Neonatal outcome assessment blinding - yes. Pregnancy outcome assessment blinding - no.
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Small loss to follow-up.
Selective reporting (reporting bias)	Low risk	Selective outcome reporting bias not detected.
Other bias	Low risk	Other bias not apparent.

Wladimiroff 1980

Methods	Randomised by booking number (even numbers to group A, odd numbers to group B).		
Participants	745 women enrolled during first antenatal care visit.		
Interventions	Single fetal chest area measurement via ultrasound between 32 to 36 weeks versus no ultrasound.		
Outcomes	Fetal chest area.		



Wladimiroff 1980 (Continued)

Notes

The primary aim of this study was to assess the ability of third trimester ultrasound in detecting small-and large-for-dates infants, and no clinical outcomes were evaluated.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	High risk	Randomised based on booking number.
Allocation concealment (selection bias)	High risk	All research staff would have known woman's status based on hospital record number.
Blinding of participants and personnel (perfor- mance bias) All outcomes	High risk	Unfeasible.
Blinding of outcome assessment (detection bias) All outcomes	High risk	Quote: 'the medical staff were informed of the ultrasonic data obtained' [where there were discrepancies in fundal height or any other abnormal antenatal finding].
Incomplete outcome data (attrition bias) All outcomes	Low risk	Small loss to follow-up.
Selective reporting (reporting bias)	Low risk	Selective outcome reporting bias not detected.
Other bias	Low risk	None found.

ELCS: elective caesarean section LGA: large-for-gestational age SGA: small-for-gestational age

Characteristics of excluded studies [ordered by study ID]

Study	Reason for exclusion	
Arzola 2013	Does not perform standard antenatal ultrasound, does not look at the effects of having an ultrasound > 24 weeks or not. This trial was simply trying to generate a model to predict gastric volume in non-fasted women based on ultrasound; outcome data not stated clearly but unlikely to be relevant.	
Hendrix 2000	Compared clinical versus ultrasound estimates of birthweight in terms of accuracy. Did not include review outcomes.	
Morrison 1992	Brief abstract. No usable data. Unclear whether this trial was completed.	
Ong 2001	Study not undertaken.	
Owen 1994	Brief abstract. No usable data. Unclear if non-randomised women were included in the analysis. Women also considered to be 'at risk' rather than unselected or low risk.	
Secher 1986	The methodology is unclear as all suspected LGA fetuses were to be referred to an obstetrician for further evaluation. However, suspected LGA in 26 such fetuses included in the final analysis was	



Study	Reason for exclusion		
	not reported to clinicians primarily because they were part of another randomised study. The other randomised trial (Secher 1987) was also not included - see reasons in this table.		
Secher 1987	In this study, third trimester ultrasound was used to identify a group of uncomplicated pregnancies where there was ultrasound suspicion of poor intrauterine growth, but no clinical suspicion of poor growth. Only these pregnancies were randomised. The revealed group underwent serial tests of fetal well being (non-stress CTG and serum oestriol and placental lactogen) and fetal growth and management was planned depending on the results of the tests. Therefore, the study assessed the value of various tests of fetal well being if fetal growth retardation was suspected, rather than the value of routine third trimester ultrasound alone.		

CTG: cardiotocograph LGA: large-for-gestational age

Characteristics of ongoing studies [ordered by study ID]

McClure 2014

Trial name or title	First Look: a cluster-randomised trial of ultrasound to improve pregnancy outcomes in low-income country settings.
Methods	Randomised controlled trial, ongoing.
Participants	All pregnant women presenting for routine antenatal care, ≥ 18 weeks and not in labour.
Interventions	Antenatal routine ultrasound 18-22 weeks' gestation and 32-36 weeks' gestation versus routine antenatal care.
Outcomes	Maternal and fetal mortality and morbidity, healthcare utilisation.
Starting date	Protocol publication: 5 February 2014.
Contact information	Elizabeth McClure mcclure@rti.org
Notes	

Verspyck 2012

Trial name or title	RECRET: Routine ultrasound screening in the third trimester.
Methods	Randomised controlled trial, ongoing.
Participants	Pregnant women at low-risk of complications, singleton only.
Interventions	Ultrasound between 34-35 weeks versus ultrasound between 30-31 weeks.
Outcomes	Small-for-gestational age, intrauterine growth restriction, healthcare utilisation outcomes, maternal and neonatal outcomes.
Starting date	May 2012.
Contact information	Eric Verspyck eric.verspyck@chu-rouen.fr



Verspyck 2012 (Continued)

Notes

DATA AND ANALYSES

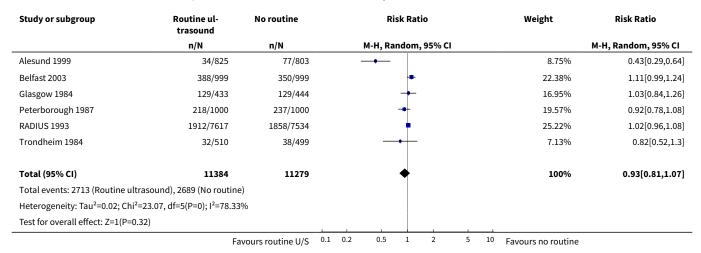
Comparison 1. Routine ultrasound > 24 weeks versus no/concealed/selective ultrasound > 24 weeks

Outcome or subgroup title	No. of studies	No. of partici- pants	Statistical method	Effect size
1 Induction of labour	6	22663	Risk Ratio (M-H, Random, 95% CI)	0.93 [0.81, 1.07]
2 Caesarean section	6	27461	Risk Ratio (M-H, Random, 95% CI)	1.03 [0.92, 1.15]
3 Perinatal mortality	8	30675	Risk Ratio (M-H, Random, 95% CI)	1.01 [0.67, 1.54]
4 Preterm delivery < 37 weeks' gestation	2	17151	Risk Ratio (M-H, Fixed, 95% CI)	0.96 [0.85, 1.08]
5 Antenatal admission	4	5396	Risk Ratio (M-H, Random, 95% CI)	1.07 [0.80, 1.43]
6 Number of days in hospital (mean, standard deviation (SD)) (non-prespecified)	1	877	Mean Difference (IV, Fixed, 95% CI)	0.10 [0.07, 0.13]
7 CTG (cardiotocograph)	1	2000	Risk Ratio (M-H, Fixed, 95% CI)	1.02 [0.97, 1.06]
8 Further ultrasound scan/s	2		Risk Ratio (M-H, Random, 95% CI)	Totals not selected
9 Instrumental delivery	5	12310	Risk Ratio (M-H, Fixed, 95% CI)	1.05 [0.95, 1.16]
10 Elective caesarean section	4	5884	Risk Ratio (M-H, Fixed, 95% CI)	1.09 [0.89, 1.34]
11 Emergency caesarean section	5	12310	Risk Ratio (M-H, Fixed, 95% CI)	1.03 [0.89, 1.20]
12 Gestation at birth (mean, SD)	3	9303	Mean Difference (IV, Random, 95% CI)	-0.10 [-0.22, 0.02]
13 Birthweight (mean, SD)	5	26136	Mean Difference (IV, Fixed, 95% CI)	4.40 [-8.89, 17.69]
14 Birthweight < 10th centile	4	20293	Risk Ratio (M-H, Random, 95% CI)	0.98 [0.74, 1.28]
15 Low birthweight < 2.5 kg	3	4510	Risk Ratio (M-H, Fixed, 95% CI)	0.92 [0.71, 1.18]
16 Neonatal resuscitation	5	12909	Risk Ratio (M-H, Fixed, 95% CI)	0.95 [0.84, 1.08]
17 Neonatal ventilation	2	3004	Risk Ratio (M-H, Random, 95% CI)	0.64 [0.23, 1.77]
18 Admission to special care baby unit	5	12915	Risk Ratio (M-H, Fixed, 95% CI)	1.01 [0.91, 1.14]
19 Apgar score < 7 at 5 minutes	4	5889	Risk Ratio (M-H, Random, 95% CI)	0.89 [0.41, 1.93]



Outcome or subgroup title	No. of studies	No. of partici- pants	Statistical method	Effect size
20 Stillbirths (non-prespecified)	6	28107	Risk Ratio (M-H, Random, 95% CI)	1.18 [0.51, 2.70]
21 Neonatal deaths	5	21708	Risk Ratio (M-H, Fixed, 95% CI)	1.04 [0.58, 1.85]
22 Perinatal mortality (excluding congenital abnormalities) (non-prespecified)	6	28133	Risk Ratio (M-H, Random, 95% CI)	1.13 [0.58, 2.19]
23 Stillbirths (excluding congenital abnormalities) (non-prespecified)	2	2902	Risk Ratio (M-H, Fixed, 95% CI)	0.05 [0.00, 0.90]
24 Neonatal deaths (excluding congenital abnormalities)	2	2902	Risk Ratio (M-H, Fixed, 95% CI)	1.99 [0.18, 21.96]
25 Post-term delivery > 42 weeks' gestation (non-prespecified)	2	17151	Risk Ratio (M-H, Fixed, 95% CI)	0.69 [0.59, 0.81]
26 Birthweight < 5th centile (non- prespecified)	2	2404	Risk Ratio (M-H, Fixed, 95% CI)	1.18 [0.81, 1.74]
27 Moderate neonatal morbidity (non-prespecified)	1	15281	Risk Ratio (M-H, Fixed, 95% CI)	0.97 [0.81, 1.16]
28 Severe neonatal morbidity (non-prespecified)	1	15281	Risk Ratio (M-H, Fixed, 95% CI)	1.03 [0.78, 1.36]
29 Perinatal mortality (twins) (non-prespecified)	3	314	Risk Ratio (M-H, Fixed, 95% CI)	0.63 [0.24, 1.66]

Analysis 1.1. Comparison 1 Routine ultrasound > 24 weeks versus no/concealed/selective ultrasound > 24 weeks, Outcome 1 Induction of labour.

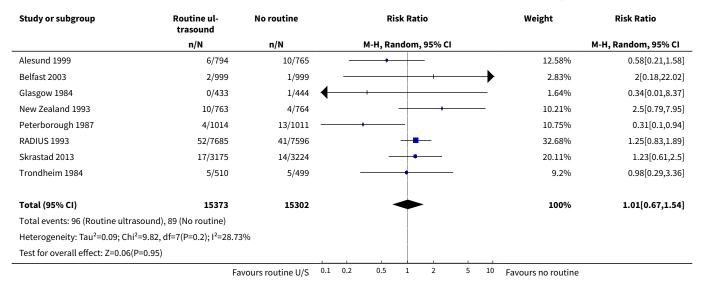




Analysis 1.2. Comparison 1 Routine ultrasound > 24 weeks versus no/concealed/selective ultrasound > 24 weeks, Outcome 2 Caesarean section.

Study or subgroup	Routine ul- trasound	No routine	Risk Ratio	Weight	Risk Ratio	
	n/N	n/N	M-H, Random, 95% CI		M-H, Random, 95% CI	
Belfast 2003	183/999	152/999	+	17.33%	1.2[0.99,1.47]	
Glasgow 1984	54/433	56/444		8.07%	0.99[0.7,1.4]	
Peterborough 1987	135/1000	140/1000		15.3%	0.96[0.77,1.2]	
RADIUS 1993	1205/7617	1135/7534	-	31.71%	1.05[0.97,1.13]	
Skrastad 2013	356/3190	409/3236	-	24.25%	0.88[0.77,1.01]	
Trondheim 1984	29/510	17/499	+	3.34%	1.67[0.93,3]	
Total (95% CI)	13749	13712	•	100%	1.03[0.92,1.15]	
Total events: 1962 (Routine ul	ltrasound), 1909 (No routine	<u>e</u>)				
Heterogeneity: Tau ² =0.01; Chi	i ² =10.79, df=5(P=0.06); I ² =53	.65%				
Test for overall effect: Z=0.49((P=0.62)					
	Fa	vours routine U/S	0.2 0.5 1 2	5 Favours no routine		

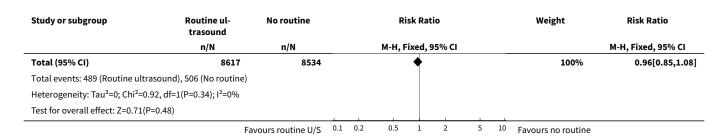
Analysis 1.3. Comparison 1 Routine ultrasound > 24 weeks versus no/concealed/selective ultrasound > 24 weeks, Outcome 3 Perinatal mortality.



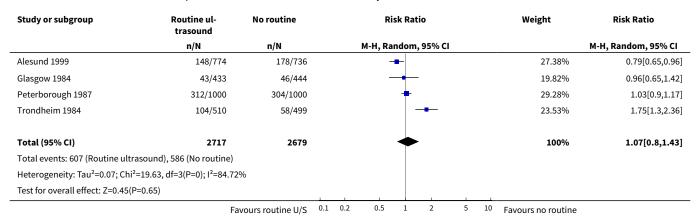
Analysis 1.4. Comparison 1 Routine ultrasound > 24 weeks versus no/concealed/ selective ultrasound > 24 weeks, Outcome 4 Preterm delivery < 37 weeks' gestation.

Study or subgroup	Routine ul- trasound	No routine	Risk Ratio				Weight	Risk Ratio			
	n/N	n/N			M-H, F	ixed,	95% CI				M-H, Fixed, 95% CI
Peterborough 1987	68/1000	61/1000				+	_			12%	1.11[0.8,1.56]
RADIUS 1993	421/7617	445/7534				+				88%	0.94[0.82,1.07]
									1		
	Fa	vours routine U/S	0.1	0.2	0.5	1	2	5	10	Favours no routine	





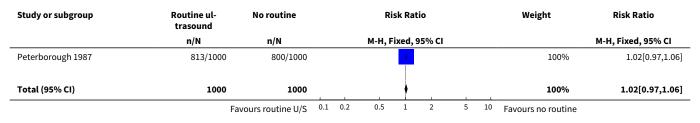
Analysis 1.5. Comparison 1 Routine ultrasound > 24 weeks versus no/concealed/selective ultrasound > 24 weeks, Outcome 5 Antenatal admission.



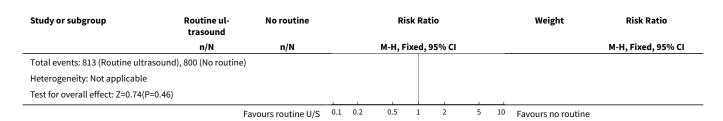
Analysis 1.6. Comparison 1 Routine ultrasound > 24 weeks versus no/concealed/selective ultrasound > 24 weeks, Outcome 6 Number of days in hospital (mean, standard deviation (SD)) (non-prespecified).

Study or subgroup	Routine	ultrasound	No routine			Mean Difference				Weight	Mean Difference
	N	Mean(SD)	N	Mean(SD)		Fi	xed, 95% C	ı			Fixed, 95% CI
Glasgow 1984	433	1 (0.2)	444	0.9 (0.2)						100%	0.1[0.07,0.13]
Total ***	433		444							100%	0.1[0.07,0.13]
Heterogeneity: Tau ² =0; Chi ² =	0, df=0(P<0.0001); I ² =100%									
Test for overall effect: Z=7.4(P<0.0001)					1					
			Favou	rs routine U/S	-10	-5	0	5	10	Favours no rout	ne

Analysis 1.7. Comparison 1 Routine ultrasound > 24 weeks versus no/concealed/selective ultrasound > 24 weeks, Outcome 7 CTG (cardiotocograph).



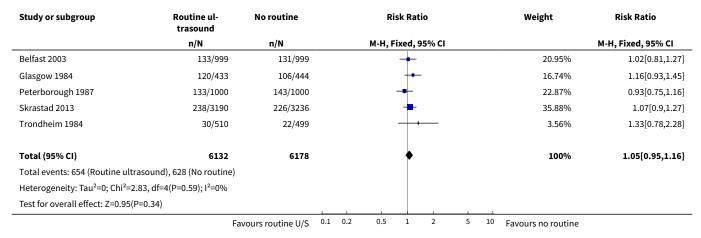




Analysis 1.8. Comparison 1 Routine ultrasound > 24 weeks versus no/concealed/selective ultrasound > 24 weeks, Outcome 8 Further ultrasound scan/s.

Study or subgroup	Routine ultrasound	No routine		Risk Ratio						Risk Ratio		
	n/N	n/N	M-H, Random, 95% CI					1	M-H, Random, 95% CI			
New Zealand 1993	149/763	236/764			+	-				0.63[0.53,0.76]		
Trondheim 1984	67/510	49/499				+				1.34[0.95,1.89]		
		Favours routine U/S	0.1	0.2	0.5	1	2	5	10	Favours no routine		

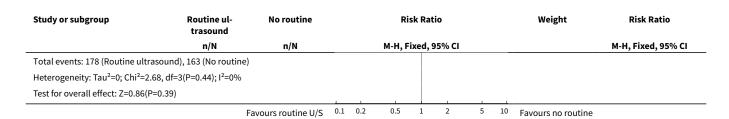
Analysis 1.9. Comparison 1 Routine ultrasound > 24 weeks versus no/concealed/selective ultrasound > 24 weeks, Outcome 9 Instrumental delivery.



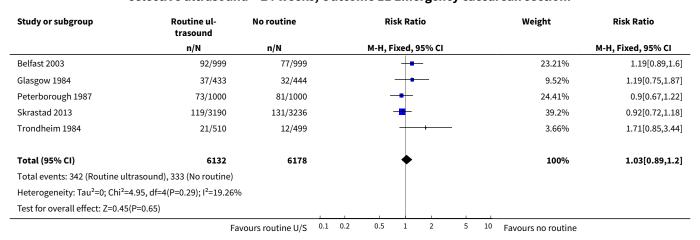
Analysis 1.10. Comparison 1 Routine ultrasound > 24 weeks versus no/concealed/ selective ultrasound > 24 weeks, Outcome 10 Elective caesarean section.

Study or subgroup	Routine ul- trasound	No routine		Risk Ratio		Weight	Risk Ratio			
	n/N	n/N		M-H, Fix	ed, 95%	CI				M-H, Fixed, 95% CI
Belfast 2003	91/999	75/999			+-				46.08%	1.21[0.91,1.63]
Glasgow 1984	17/433	24/444			 				14.56%	0.73[0.4,1.33]
Peterborough 1987	62/1000	59/1000		_	<u> </u>				36.25%	1.05[0.74,1.48]
Trondheim 1984	8/510	5/499			+-		-		3.11%	1.57[0.52,4.75]
Total (95% CI)	2942	2942			•				100%	1.09[0.89,1.34]
	Fa	vours routine U/S	0.1 0.2	0.5	1 2		5	10	Favours no routine	





Analysis 1.11. Comparison 1 Routine ultrasound > 24 weeks versus no/concealed/ selective ultrasound > 24 weeks, Outcome 11 Emergency caesarean section.



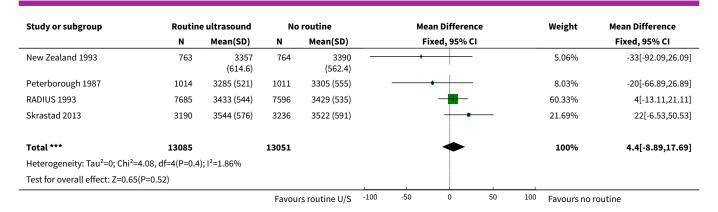
Analysis 1.12. Comparison 1 Routine ultrasound > 24 weeks versus no/concealed/ selective ultrasound > 24 weeks, Outcome 12 Gestation at birth (mean, SD).

Study or subgroup	Routin	e ultrasound	No	routine		Mean Difference			Weight	Mean Difference	
	N	Mean(SD)	N	Mean(SD)		Rai	ndom, 95% CI				Random, 95% CI
Glasgow 1984	433	39.3 (1.2)	444	39.5 (1.2)			-			28.05%	-0.2[-0.36,-0.04]
Peterborough 1987	1000	39.1 (1.6)	1000	39.2 (1.6)						31.66%	-0.13[-0.27,0.01]
Skrastad 2013	3190	40 (1.9)	3236	40 (2)			•			40.3%	0[-0.1,0.1]
Total ***	4623		4680				•			100%	-0.1[-0.22,0.02]
Heterogeneity: Tau ² =0.01; Ch	ni²=5.36, df=2(P=	0.07); I ² =62.66%)								
Test for overall effect: Z=1.56	(P=0.12)										
			Favou	rs routine U/S	-5	-2.5	0	2.5	5	Favours no i	outine

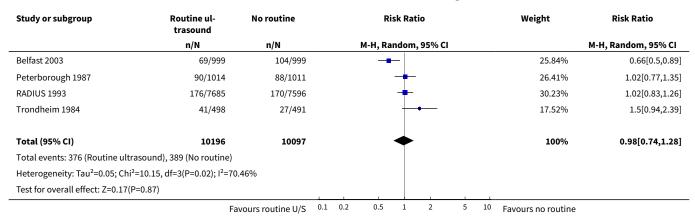
Analysis 1.13. Comparison 1 Routine ultrasound > 24 weeks versus no/concealed/selective ultrasound > 24 weeks, Outcome 13 Birthweight (mean, SD).

Study or subgroup	Routine	ultrasound	No routine			Mean Difference				Weight	Mean Difference
	N	Mean(SD)	N	Mean(SD)	Fixed, 95% CI				Fixed, 95% CI		
Glasgow 1984	433	3430 (500)	444	3420 (400)		_	+			4.9%	10[-50.02,70.02]
			Favou	rs routine U/S	-100	-50	0	50	100	Favours no re	outine

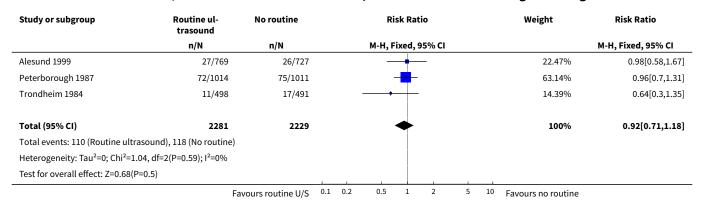




Analysis 1.14. Comparison 1 Routine ultrasound > 24 weeks versus no/concealed/ selective ultrasound > 24 weeks, Outcome 14 Birthweight < 10th centile.



Analysis 1.15. Comparison 1 Routine ultrasound > 24 weeks versus no/concealed/selective ultrasound > 24 weeks, Outcome 15 Low birthweight < 2.5 kg.

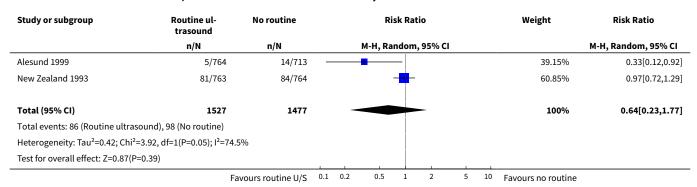




Analysis 1.16. Comparison 1 Routine ultrasound > 24 weeks versus no/concealed/selective ultrasound > 24 weeks, Outcome 16 Neonatal resuscitation.

Study or subgroup	Routine ul- trasound	No routine		Risk Ratio			Weight	Risk Ratio			
	n/N	n/N			M-H, F	ixed, 9	5% CI				M-H, Fixed, 95% CI
Belfast 2003	70/993	71/999				+				16.54%	0.99[0.72,1.36]
New Zealand 1993	184/763	202/764				-				47.16%	0.91[0.77,1.08]
Peterborough 1987	20/1014	17/1011			_	+				3.98%	1.17[0.62,2.23]
Skrastad 2013	105/3163	111/3213				+				25.73%	0.96[0.74,1.25]
Trondheim 1984	28/498	28/491			_	+	_			6.59%	0.99[0.59,1.64]
Total (95% CI)	6431	6478				•				100%	0.95[0.84,1.08]
Total events: 407 (Routine ultr	asound), 429 (No routine)										
Heterogeneity: Tau ² =0; Chi ² =0	.73, df=4(P=0.95); I ² =0%										
Test for overall effect: Z=0.75(F	P=0.45)										
	Fa	vours routine U/S	0.1	0.2	0.5	1	2	5	10	Favours no routine	

Analysis 1.17. Comparison 1 Routine ultrasound > 24 weeks versus no/concealed/selective ultrasound > 24 weeks, Outcome 17 Neonatal ventilation.

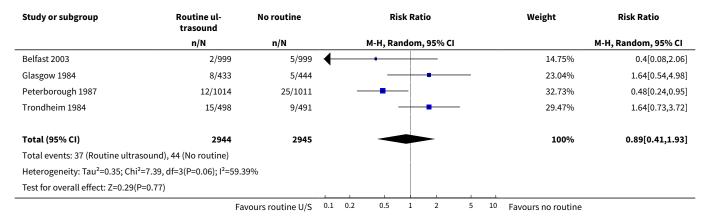


Analysis 1.18. Comparison 1 Routine ultrasound > 24 weeks versus no/concealed/selective ultrasound > 24 weeks, Outcome 18 Admission to special care baby unit.

Study or subgroup	Routine ul- trasound	No routine		Risk Ratio		Weight	Risk Ratio
	n/N	n/N		M-H, Fixed, 95% CI			M-H, Fixed, 95% CI
Belfast 2003	28/999	34/999				6.44%	0.82[0.5,1.35]
New Zealand 1993	107/763	94/764		+		17.8%	1.14[0.88,1.48]
Peterborough 1987	48/1014	60/1011		+		11.39%	0.8[0.55,1.15]
Skrastad 2013	333/3163	320/3213		 		60.17%	1.06[0.91,1.22]
Trondheim 1984	17/498	22/491		+		4.2%	0.76[0.41,1.42]
Total (95% CI)	6437	6478		•		100%	1.01[0.91,1.14]
Total events: 533 (Routine ulti	rasound), 530 (No routine)						
Heterogeneity: Tau ² =0; Chi ² =4	1.22, df=4(P=0.38); I ² =5.28%						
Test for overall effect: Z=0.25(P=0.8)						
	Fa	vours routine U/S	0.1 0.2	0.5 1 2	5 10	Favours no routine	



Analysis 1.19. Comparison 1 Routine ultrasound > 24 weeks versus no/concealed/ selective ultrasound > 24 weeks, Outcome 19 Apgar score < 7 at 5 minutes.



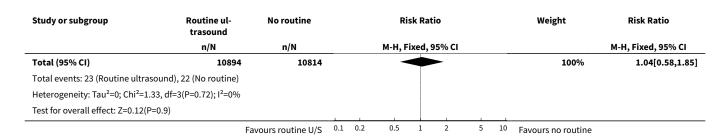
Analysis 1.20. Comparison 1 Routine ultrasound > 24 weeks versus no/concealed/selective ultrasound > 24 weeks, Outcome 20 Stillbirths (non-prespecified).

Study or subgroup	Routine ul- trasound	No routine		Risk Ratio	o	Weight	Risk Ratio
	n/N	n/N		M-H, Random,	95% CI		M-H, Random, 95% CI
Belfast 2003	2/999	1/999	_		*	9.2%	2[0.18,22.02]
Glasgow 1984	0/433	0/444					Not estimable
New Zealand 1993	8/763	2/764		-	+	16.66%	4.01[0.85,18.8]
Peterborough 1987	1/1014	12/1011	\leftarrow			11.69%	0.08[0.01,0.64]
RADIUS 1993	34/7685	23/7596		+-		33.93%	1.46[0.86,2.48]
Skrastad 2013	12/3175	11/3224		-		28.51%	1.11[0.49,2.51]
Total (95% CI)	14069	14038				100%	1.18[0.51,2.7]
Total events: 57 (Routine ultra	asound), 49 (No routine)						
Heterogeneity: Tau ² =0.46; Chi	² =9.84, df=4(P=0.04); l ² =59.3	15%					
Test for overall effect: Z=0.38(P=0.7)					1	
	Fa	vours routine U/S	0.1 0.2	0.5 1	2 5 1	Favours no routine	

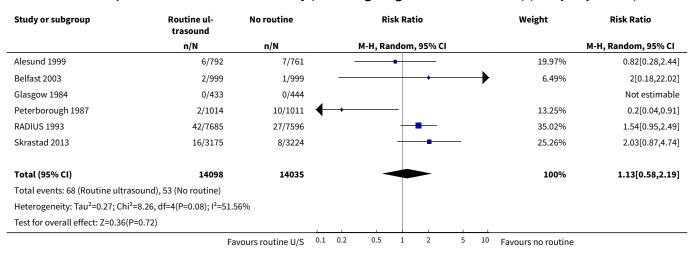
Analysis 1.21. Comparison 1 Routine ultrasound > 24 weeks versus no/concealed/selective ultrasound > 24 weeks, Outcome 21 Neonatal deaths.

Study or subgroup	Routine ul- trasound	No routine			Ri	sk Ra	tio			Weight	Risk Ratio
	n/N	n/N			M-H, F	ixed,	95% CI				M-H, Fixed, 95% CI
Belfast 2003	0/999	0/999									Not estimable
Glasgow 1984	0/433	1/444	+		+				_	6.56%	0.34[0.01,8.37]
New Zealand 1993	2/763	2/764				+			-	8.85%	1[0.14,7.09]
Peterborough 1987	3/1014	1/1011				+	+		→	4.43%	2.99[0.31,28.71]
RADIUS 1993	18/7685	18/7596			_		_			80.16%	0.99[0.51,1.9]
				1					1		
	Fa	vours routine U/S	0.1	0.2	0.5	1	2	5	10	Favours no routine	

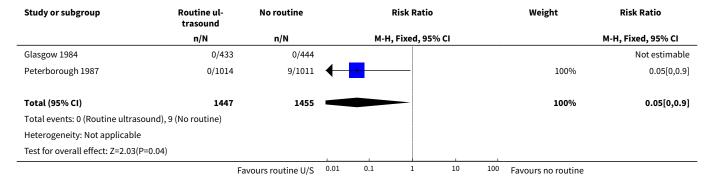




Analysis 1.22. Comparison 1 Routine ultrasound > 24 weeks versus no/concealed/selective ultrasound > 24 weeks, Outcome 22 Perinatal mortality (excluding congenital abnormalities) (non-prespecified).

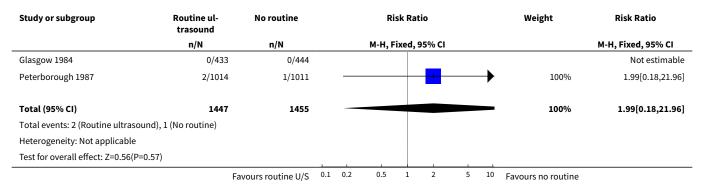


Analysis 1.23. Comparison 1 Routine ultrasound > 24 weeks versus no/concealed/selective ultrasound > 24 weeks, Outcome 23 Stillbirths (excluding congenital abnormalities) (non-prespecified).

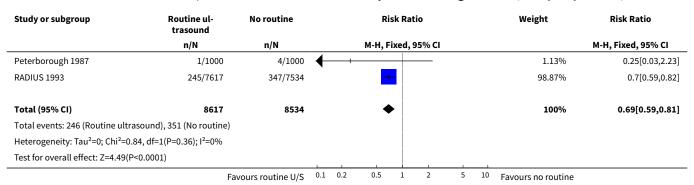




Analysis 1.24. Comparison 1 Routine ultrasound > 24 weeks versus no/concealed/selective ultrasound > 24 weeks, Outcome 24 Neonatal deaths (excluding congenital abnormalities).



Analysis 1.25. Comparison 1 Routine ultrasound > 24 weeks versus no/concealed/selective ultrasound > 24 weeks, Outcome 25 Post-term delivery > 42 weeks' gestation (non-prespecified).

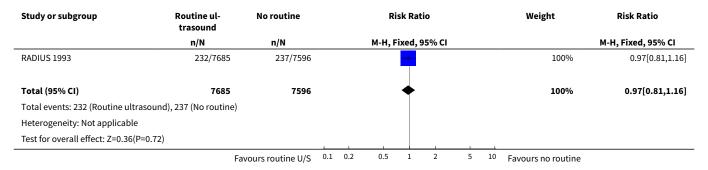


Analysis 1.26. Comparison 1 Routine ultrasound > 24 weeks versus no/concealed/selective ultrasound > 24 weeks, Outcome 26 Birthweight < 5th centile (non-prespecified).

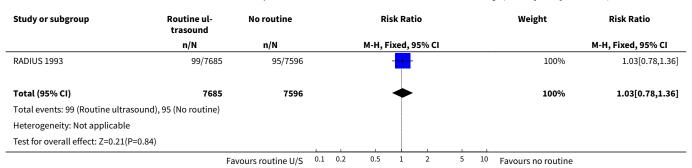
Study or subgroup	Routine ul- trasound	No routine			Ri	sk Rat	io			Weight	Risk Ratio
	n/N	n/N			M-H, F	ixed, 9	95% CI				M-H, Fixed, 95% CI
Glasgow 1984	17/433	16/444			_	-				34.51%	1.09[0.56,2.13]
New Zealand 1993	37/763	30/764				+	<u> </u>			65.49%	1.23[0.77,1.98]
Total (95% CI)	1196	1208					-			100%	1.18[0.81,1.74]
Total events: 54 (Routine ultra	asound), 46 (No routine)										
Heterogeneity: Tau ² =0; Chi ² =0	0.09, df=1(P=0.76); I ² =0%										
Test for overall effect: Z=0.86((P=0.39)										
	Fa	vours routine U/S	0.1	0.2	0.5	1	2	5	10	Favours no routine	



Analysis 1.27. Comparison 1 Routine ultrasound > 24 weeks versus no/concealed/selective ultrasound > 24 weeks, Outcome 27 Moderate neonatal morbidity (non-prespecified).



Analysis 1.28. Comparison 1 Routine ultrasound > 24 weeks versus no/concealed/selective ultrasound > 24 weeks, Outcome 28 Severe neonatal morbidity (non-prespecified).



Analysis 1.29. Comparison 1 Routine ultrasound > 24 weeks versus no/concealed/selective ultrasound > 24 weeks, Outcome 29 Perinatal mortality (twins) (non-prespecified).

Study or subgroup	Routine ul- trasound					Weight	Risk Ratio				
	n/N	n/N			M-H, F	ixed, 9	95% CI				M-H, Fixed, 95% CI
Alesund 1999	2/20	2/15	_			•				24.21%	0.75[0.12,4.73]
RADIUS 1993	4/136	4/123		_		-		-		44.49%	0.9[0.23,3.54]
Trondheim 1984	0/12	2/8	 							31.29%	0.14[0.01,2.55]
Total (95% CI)	168	146		_			-			100%	0.63[0.24,1.66]
Total events: 6 (Routine ultras	ound), 8 (No routine)										
Heterogeneity: Tau ² =0; Chi ² =1	34, df=2(P=0.51); I ² =0%										
Test for overall effect: Z=0.94(I	P=0.35)										
	Fa	vours routine U/S	0.1	0.2	0.5	1	2	5	10	Favours no routine	

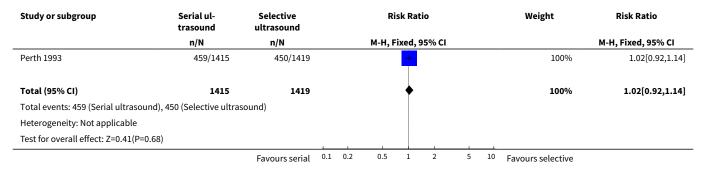


Comparison 2. Serial ultrasound and Doppler ultrasound versus selective ultrasound

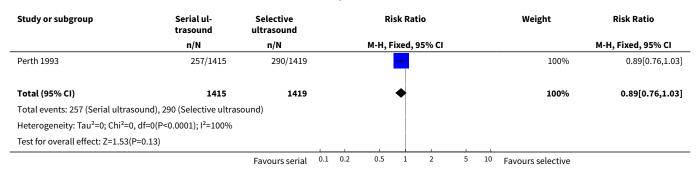
Outcome or subgroup title	No. of studies	No. of partici- pants	Statistical method	Effect size
1 Induction of labour	1	2834	Risk Ratio (M-H, Fixed, 95% CI)	1.02 [0.92, 1.14]
2 Caesarean section	1	2834	Risk Ratio (M-H, Fixed, 95% CI)	0.89 [0.76, 1.03]
3 Perinatal mortality	1	2834	Risk Ratio (M-H, Fixed, 95% CI)	0.59 [0.30, 1.17]
4 CTG (cardiograph)	1	2834	Risk Ratio (M-H, Fixed, 95% CI)	1.01 [0.93, 1.09]
5 Elective caesarean section	1	2834	Risk Ratio (M-H, Fixed, 95% CI)	0.95 [0.77, 1.17]
6 Emergency caesarean section	1	2834	Risk Ratio (M-H, Fixed, 95% CI)	0.82 [0.64, 1.05]
7 Gestation at birth (mean, SD)	1	2834	Mean Difference (IV, Fixed, 95% CI)	-0.10 [-1.21, 1.01]
8 Birthweight (mean, SD)	1	2834	Mean Difference (IV, Fixed, 95% CI)	-25.0 [-67.53, 17.53]
9 Birthweight < 10th centile	1	2834	Risk Ratio (M-H, Fixed, 95% CI)	1.36 [1.10, 1.68]
10 Birthweight < 3rd centile	1	2834	Risk Ratio (M-H, Fixed, 95% CI)	1.66 [1.10, 2.51]
11 Low birthweight (< 2.5 kg)	1	2834	Risk Ratio (M-H, Fixed, 95% CI)	1.14 [0.85, 1.52]
12 Very low birthweight (< 1.5 kg)	1	2834	Risk Ratio (M-H, Fixed, 95% CI)	1.27 [0.65, 2.49]
13 Need for resuscitation	1	2834	Risk Ratio (M-H, Fixed, 95% CI)	0.98 [0.92, 1.05]
14 Need for ventilation	1	2834	Risk Ratio (M-H, Fixed, 95% CI)	0.67 [0.41, 1.09]
15 Admission to special care baby unit	2	2979	Risk Ratio (M-H, Fixed, 95% CI)	0.95 [0.69, 1.30]
16 Apgar score < 7 at 5 minutes	1	2834	Risk Ratio (M-H, Fixed, 95% CI)	0.77 [0.46, 1.27]
17 Neonatal intraventricular haemorrhage	1	2834	Risk Ratio (M-H, Fixed, 95% CI)	0.80 [0.22, 2.98]
18 Stillbirths	1	2834	Risk Ratio (M-H, Fixed, 95% CI)	0.84 [0.36, 1.93]
19 Neonatal deaths (non-prespecified)	1	2834	Risk Ratio (M-H, Fixed, 95% CI)	0.30 [0.08, 1.09]
20 Neonatal deaths (excluding congenital abnormalities) (non-prespecified)	1	2834	Risk Ratio (M-H, Fixed, 95% CI)	0.40 [0.08, 2.06]



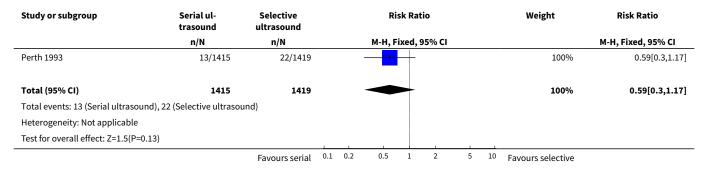
Analysis 2.1. Comparison 2 Serial ultrasound and Doppler ultrasound versus selective ultrasound, Outcome 1 Induction of labour.



Analysis 2.2. Comparison 2 Serial ultrasound and Doppler ultrasound versus selective ultrasound, Outcome 2 Caesarean section.

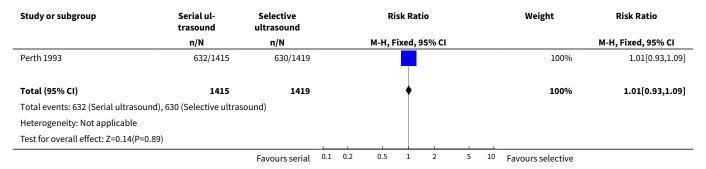


Analysis 2.3. Comparison 2 Serial ultrasound and Doppler ultrasound versus selective ultrasound, Outcome 3 Perinatal mortality.

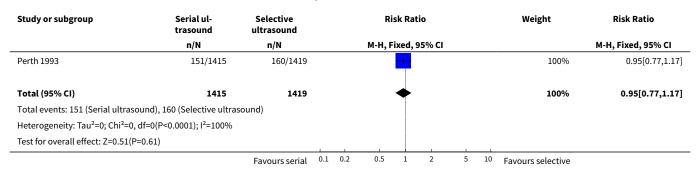




Analysis 2.4. Comparison 2 Serial ultrasound and Doppler ultrasound versus selective ultrasound, Outcome 4 CTG (cardiograph).



Analysis 2.5. Comparison 2 Serial ultrasound and Doppler ultrasound versus selective ultrasound, Outcome 5 Elective caesarean section.



Analysis 2.6. Comparison 2 Serial ultrasound and Doppler ultrasound versus selective ultrasound, Outcome 6 Emergency caesarean section.

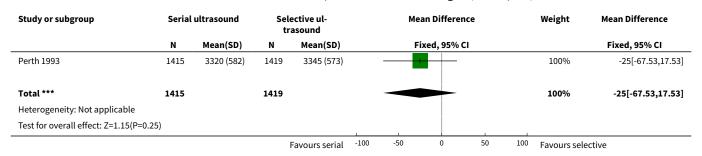
Study or subgroup	Serial ul- trasound	Selective ultrasound			Ri	sk Rat	io			Weight	Risk Ratio
	n/N	n/N			M-H, F	ixed,	95% CI				M-H, Fixed, 95% CI
Perth 1993	106/1415	130/1419			-	-				100%	0.82[0.64,1.05]
Total (95% CI)	1415	1419			•					100%	0.82[0.64,1.05]
Total events: 106 (Serial ultrasound), 3	130 (Selective ultras	sound)									
Heterogeneity: Not applicable											
Test for overall effect: Z=1.61(P=0.11)											
		Favours serial	0.1	0.2	0.5	1	2	5	10	Favours selective	



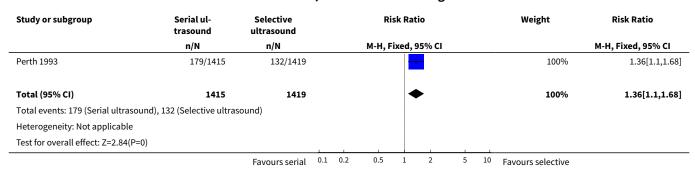
Analysis 2.7. Comparison 2 Serial ultrasound and Doppler ultrasound versus selective ultrasound, Outcome 7 Gestation at birth (mean, SD).

Study or subgroup	Serial	ultrasound	Selective ul- trasound			Mean Difference				Weight	Mean Difference
	N	Mean(SD)	N	Mean(SD)		F	ixed, 95% CI				Fixed, 95% CI
Perth 1993	1415	274.7 (14.5)	1419	274.8 (15.5)						100%	-0.1[-1.21,1.01]
Total ***	1415		1419				•			100%	-0.1[-1.21,1.01]
Heterogeneity: Tau ² =0; Chi ² =	=0, df=0(P<0.0001	1); I ² =100%									
Test for overall effect: Z=0.18	3(P=0.86)										
				Favours serial	-10	-5	0	5	10	Favours selectiv	e

Analysis 2.8. Comparison 2 Serial ultrasound and Doppler ultrasound versus selective ultrasound, Outcome 8 Birthweight (mean, SD).



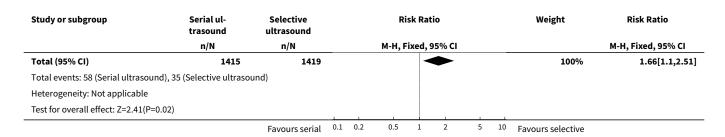
Analysis 2.9. Comparison 2 Serial ultrasound and Doppler ultrasound versus selective ultrasound, Outcome 9 Birthweight < 10th centile.



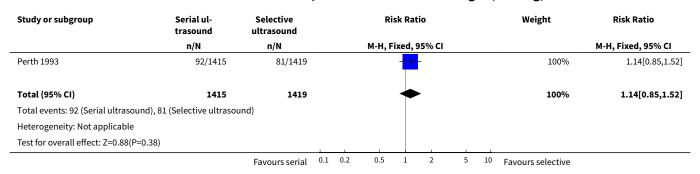
Analysis 2.10. Comparison 2 Serial ultrasound and Doppler ultrasound versus selective ultrasound, Outcome 10 Birthweight < 3rd centile.

Study or subgroup	Serial ul- trasound	Selective ultrasound		Risk Ratio						Weight	Risk Ratio
	n/N	n/N			M-H, F	ixed,	95% CI				M-H, Fixed, 95% CI
Perth 1993	58/1415	35/1419				-	1			100%	1.66[1.1,2.51]
		Favours serial	0.1	0.2	0.5	1	2	5	10	Favours selective	

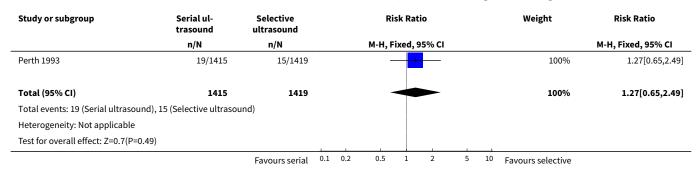




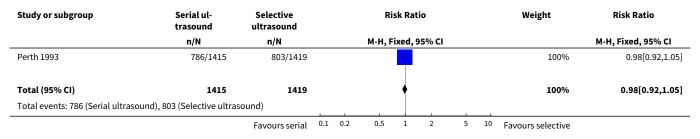
Analysis 2.11. Comparison 2 Serial ultrasound and Doppler ultrasound versus selective ultrasound, Outcome 11 Low birthweight (< 2.5 kg).



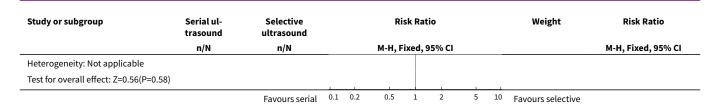
Analysis 2.12. Comparison 2 Serial ultrasound and Doppler ultrasound versus selective ultrasound, Outcome 12 Very low birthweight (< 1.5 kg).



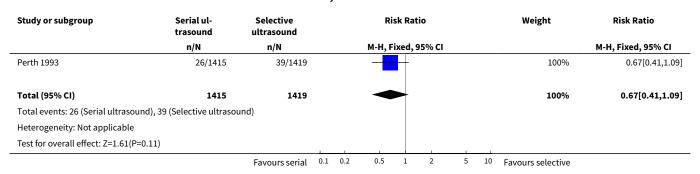
Analysis 2.13. Comparison 2 Serial ultrasound and Doppler ultrasound versus selective ultrasound, Outcome 13 Need for resuscitation.







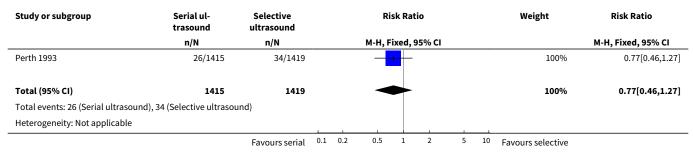
Analysis 2.14. Comparison 2 Serial ultrasound and Doppler ultrasound versus selective ultrasound, Outcome 14 Need for ventilation.



Analysis 2.15. Comparison 2 Serial ultrasound and Doppler ultrasound versus selective ultrasound, Outcome 15 Admission to special care baby unit.

Study or subgroup	Serial ul- trasound	Selective ultrasound			Ri	isk Rati	io			Weight	Risk Ratio
	n/N	n/N			M-H, F	ixed, 9	5% CI				M-H, Fixed, 95% CI
Ellwood 1997	5/61	7/84				+				7.77%	0.98[0.33,2.95]
Perth 1993	66/1415	70/1419			-	-				92.23%	0.95[0.68,1.31]
Total (95% CI)	1476	1503				•				100%	0.95[0.69,1.3]
Total events: 71 (Serial ultraso	ound), 77 (Selective ultrasou	ınd)									
Heterogeneity: Tau ² =0; Chi ² =0	, df=1(P=0.95); I ² =0%										
Test for overall effect: Z=0.33(F	P=0.74)										
		Favours serial	0.1	0.2	0.5	1	2	5	10	Favours selective	

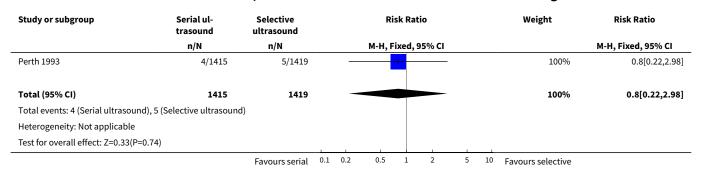
Analysis 2.16. Comparison 2 Serial ultrasound and Doppler ultrasound versus selective ultrasound, Outcome 16 Apgar score < 7 at 5 minutes.



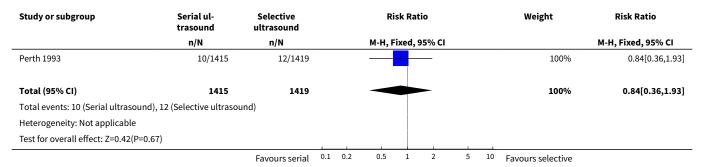


Study or subgroup	Serial ul- trasound	Selective ultrasound			Ri	sk Ra	tio			Weight	Risk Ratio
	n/N	n/N			M-H, F	ixed,	95% CI				M-H, Fixed, 95% CI
Test for overall effect: Z=1.03(P=0.3)											
		Favours serial	0.1	0.2	0.5	1	2	5	10	Favours selective	

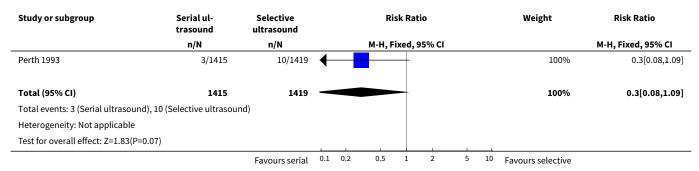
Analysis 2.17. Comparison 2 Serial ultrasound and Doppler ultrasound versus selective ultrasound, Outcome 17 Neonatal intraventricular haemorrhage.



Analysis 2.18. Comparison 2 Serial ultrasound and Doppler ultrasound versus selective ultrasound, Outcome 18 Stillbirths.

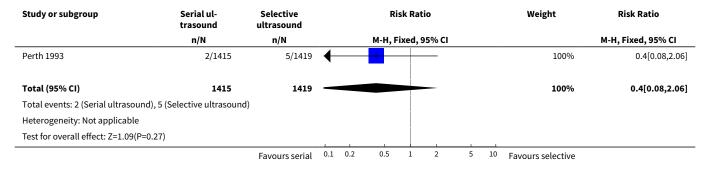


Analysis 2.19. Comparison 2 Serial ultrasound and Doppler ultrasound versus selective ultrasound, Outcome 19 Neonatal deaths (non-prespecified).





Analysis 2.20. Comparison 2 Serial ultrasound and Doppler ultrasound versus selective ultrasound, Outcome 20 Neonatal deaths (excluding congenital abnormalities) (non-prespecified).



WHAT'S NEW

Date	Event	Description
31 May 2015	New search has been performed	Search updated and seven new reports identified. Two new trials were included. Two reports were additional publications for a previously included study; one report was excluded, and two reports have been placed in Ongoing studies.
		Two studies previously excluded for no data have been moved to included studies because it is no longer the practice to exclude otherwise eligible trials based on a lack of outcome data alone (Belanger 1996; Wladimiroff 1980).
31 May 2015	New citation required but conclusions have not changed	Search updated and conclusions not changed. Methods updated and 'Summary of findings' table added.

HISTORY

Protocol first published: Issue 2, 1999 Review first published: Issue 1, 2000

Date	Event	Description
13 May 2009	Amended	No changes - republished to fix technical problem.
28 May 2008	New search has been performed	We updated the search in February 2008 and identified an additional trial (Belfast 2003). We updated the methods, included risk of bias tables and updated the analyses. There are some small changes in the results but there are no substantial changes to the conclusions.
28 May 2008	New citation required but conclusions have not changed	A new author joined the review team to prepare this update.
26 February 2008	Amended	Converted to new review format.



Date	Event	Description
5 February 2007	Amended	Review withdrawn from publication.

CONTRIBUTIONS OF AUTHORS

Leanne Bricker drafted the original review. For the 2015 update, Nancy Medley and Jeremy Pratt assessed new studies for inclusion, extracted data, updated methods, prepared a 'Summary of findings' table and edited the text of the review. Leanne Bricker advised on the update of the review and edited the final draft of the review.

DECLARATIONS OF INTEREST

None known.

SOURCES OF SUPPORT

Internal sources

• The University of Liverpool, UK.

External sources

• National Institute for Health Research, UK.

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• UNDP/UNFPA/UNICEF/WHO/World Bank Special Programme of Research, Development and Research Training in Human Reproduction (HRP), Department of Reproductive Health and Research (RHR), World Health Organization, Switzerland.

DIFFERENCES BETWEEN PROTOCOL AND REVIEW

The following non-prespecified outcome measures were used.

- 1. Post-term delivery greater than 42 weeks.
- 2. Birthweight less than 5th percentile.
- 3. Moderate neonatal morbidity (includes any of the following: presumed neonatal sepsis, oxygen required greater than 48 hours, necrotising enterocolitis without perforation, grade I or II intraventricular haemorrhage (IVH), fracture of clavicle or other bones, facial nerve injury, brachial plexus injury, stay greater than five days in the special care nursery).
- 4. Severe neonatal morbidity (includes any of the following: grade IV retinopathy of prematurity, bronchopulmonary dysplasia, mechanical ventilation greater than 48 hours, intestinal perforation due to necrotising enterocolitis, grade III or IV IVH, subdural or cerebral haemorrhage, spinal cord injury, neonatal seizures, placement of chest tube, documented neonatal sepsis, and stay more than 30 days in the special care nursery).
- 5. Neonatal deaths.
- 6. Stillbirths.
- 7. Perinatal mortality of twins.
- 8. Perinatal mortality (excluding congenital abnormalities)
- 9. Stillbirths (excluding congenital abnormalities)
- 10. Neonatal deaths (excluding congenital abnormalities)
- 11. Number of days in hospital

Preterm delivery less than 37 weeks was added as a non-prespecified primary outcome for the 2015 update.

INDEX TERMS

Medical Subject Headings (MeSH)

*Pregnancy Outcome; *Ultrasonography, Prenatal; Perinatal Mortality; Pregnancy Trimester, Second; Pregnancy Trimester, Third; Premature Birth [epidemiology]; Randomized Controlled Trials as Topic



MeSH check words

Female; Humans; Infant, Newborn; Pregnancy